

# WEST Search History

DATE: Thursday, November 06, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>			
L8	Pronectin adj F and composition?	17	L8
L7	Pronectin adj F	22	L7
L6	repeat\$ adj RGD	8	L6
L5	repeating adj RGD	0	L5
L4	RGD same (repeat\$ and composition?)	29	L4
L3	RGD same repeat\$	247	L3
L2	RGD same (repeat\$ and polymer?)	16	L2
L1	RGD same (repeat\$ or motif or polymer?)	884	L1

END OF SEARCH HISTORY

## WEST Search History

DATE: Thursday, November 06, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,EPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=ADJ</i>			
L4	RGD same (repeat\$ and composition?)	29	L4
L3	RGD same repeat\$	247	L3
L2	RGD same (repeat\$ and polymer?)	16	L2
L1	RGD same (repeat\$ or motif or polymer?)	884	L1

END OF SEARCH HISTORY

**WEST**[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 29 of 29 returned.****1. Document ID: US 20030144230 A1**

L4: Entry 1 of 29

File: PGPB

Jul 31, 2003

PGPUB-DOCUMENT-NUMBER: 20030144230

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030144230 A1

TITLE: Peptide-enhanced transfections

PUBLICATION-DATE: July 31, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hawley-Nelson, Pamela	Silver Spring	MD	US	
Lan, Jianqing	Germantown	MD	US	
Shih, PoJen	Columbia	MD	US	
Jessee, Joel A.	Mt. Airy	MD	US	
Schifferli, Kevin P.	Germantown	MD	US	
Gebeyehu, Gulilat	Silver Spring	MD	US	
Ciccarone, Valentina C.	Gaithersburg	MD	US	
Evans, Krista L.	Germantown	MD	US	

US-CL-CURRENT: [514/44](#); [435/458](#)

<a href="#">Full</a>	<a href="#">Title</a>	<a href="#">Citation</a>	<a href="#">Front</a>	<a href="#">Review</a>	<a href="#">Classification</a>	<a href="#">Date</a>	<a href="#">Reference</a>	<a href="#">Sequences</a>	<a href="#">Attachments</a>
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<a href="#">Full</a>	<a href="#">Draw</a>	<a href="#">Draw</a>	<a href="#">Image</a>
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**2. Document ID: US 20030069173 A1**

L4: Entry 2 of 29

File: PGPB

Apr 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030069173

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030069173 A1

TITLE: Peptide-enhanced transfections

PUBLICATION-DATE: April 10, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hawley-Nelson, Pamela	Silver Spring	MD	US	
Lan, Jianqing	Germantown	MD	US	
Shih, PoJen	Columbia	MD	US	
Jessee, Joel A.	Mt. Airy	MD	US	
Schifferli, Kevin P.	Germantown	MD	US	
Gebeyehu, Gulilat	Silver Spring	MD	US	
Ciccarone, Valentina C.	Gaithersburg	MD	US	
Evans, Krista L.	Germantown	MD	US	

US-CL-CURRENT: 514/8; 435/458, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachment
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## 3. Document ID: US 20030013655 A1

L4: Entry 3 of 29

File: PGPB

Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013655  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030013655 A1

TITLE: Compounds and methods for regulating cell adhesion

PUBLICATION-DATE: January 16, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Blaschuk, Orest W.	Westmount		CA	
Gour, Barbara J.	Beaconsfield		CA	

US-CL-CURRENT: 514/14; 514/15, 514/16, 514/17, 514/18

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachment
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## 4. Document ID: US 20020182241 A1

L4: Entry 4 of 29

File: PGPB

Dec 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020182241  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020182241 A1

TITLE: Tissue engineering of three-dimensional vascularized using microfabricated polymer assembly technology

PUBLICATION-DATE: December 5, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Borenstein, Jeffrey T.	Cambridge	MA	US	
King, Kevin R.	Cambridge	MA	US	
Terai, Hidetomi	Osaka	MA	JP	
Vacanti, Joseph P.	Boston		US	

US-CL-CURRENT: 424/422; 428/188, 435/69.4, 536/56

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 5. Document ID: US 20020169280 A1

L4: Entry 5 of 29

File: PGPB

Nov 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020169280  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020169280 A1

TITLE: Methods and compositions for inhibiting endothelial cell and fibrinogen mediated inflammation

PUBLICATION-DATE: November 14, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Altieri, Dario C.	La Jolla	CA	US	
Languino, Lucia R.	La Jolla	CA	US	
Thornton, George B.	Ramona	CA	US	

US-CL-CURRENT: 530/325; 530/324, 530/326, 530/388.24

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 6. Document ID: US 20020131970 A1

L4: Entry 6 of 29

File: PGPB

Sep 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020131970  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020131970 A1

TITLE: Methods and compositions for inhibiting endothelial cell and fibrinogen mediated inflammation

PUBLICATION-DATE: September 19, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Altieri, Dario C.	La Jolla	CA	US	
Languino, Lucia R.	La Jolla	CA	US	
Thornton, George B.	Ramona	CA	US	

US-CL-CURRENT: 424/155.1; 530/387.9

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 7. Document ID: US 20010027237 A1

L4: Entry 7 of 29

File: PGPB

Oct 4, 2001

PGPUB-DOCUMENT-NUMBER: 20010027237

PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20010027237 A1

TITLE: Comb copolymers for regulating cell-surface interactions

PUBLICATION-DATE: October 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Mayes, Anne M.	Waltham	MA	US	
Griffith, Linda G.	Cambridge	MA	US	
Irvine, Darrell J.	Cambridge	MA	US	
Banerjee, Pallab	Boston	MA	US	
Johnson, Terry D.	Allston	MA	US	

US-CL-CURRENT: 525/326.1; 424/422, 424/78.08, 424/78.17, 424/78.18, 525/418, 525/474

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequence	Attachment
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8. Document ID: US 6399700 B2

L4: Entry 8 of 29

File: USPT

Jun 4, 2002

US-PAT-NO: 6399700  
DOCUMENT-IDENTIFIER: US 6399700 B2

TITLE: Comb copolymers for regulating cell-surface interactions

DATE-ISSUED: June 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 524/731; 427/2.1, 427/2.12, 427/2.13, 435/325, 435/373, 435/374,  
435/375, 435/378, 435/395, 435/396, 435/402, 435/404, 524/732, 525/165, 525/166,  
525/168, 525/54.1, 525/54.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequence	Attachment
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9. Document ID: US 6376248 B1

L4: Entry 9 of 29

File: USPT

Apr 23, 2002

US-PAT-NO: 6376248  
DOCUMENT-IDENTIFIER: US 6376248 B1

TITLE: Peptide-enhanced transfections

DATE-ISSUED: April 23, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hawley-Nelson; Pamela	Silver Spring	MD		
Lan; Jiangqing	Germantown	MD		
Shih; PoJen	Columbia	MD		
Jessee; Joel A.	Mt. Airy	MD		
Schifferli; Kevin P.	Germantown	MD		
Gebeyehu; Gulilat	Silver Spring	MD		
Ciccarone; Valentina C.	Gaithersburg	MD		
Evans; Krista L.	Germantown	MD		

US-CL-CURRENT: 435/458; 435/235.1, 435/320.1, 536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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## 10. Document ID: US 6316412 B1

L4: Entry 10 of 29

File: USPT

Nov 13, 2001

US-PAT-NO: 6316412

DOCUMENT-IDENTIFIER: US 6316412 B1

TITLE: Polypeptides for promoting cell attachment

DATE-ISSUED: November 13, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ginsberg; Mark H.	San Diego	CA		
Plow; Edward F.	San Diego	CA		
Bowditch; Ronald	Encinitas	CA		

US-CL-CURRENT: 514/15; 514/12, 530/300, 530/324, 530/325, 530/326, 530/327, 530/328, 530/329, 530/330, 530/350, 530/387.1, 530/387.9

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 11. Document ID: US 6310177 B1

L4: Entry 11 of 29

File: USPT

Oct 30, 2001

US-PAT-NO: 6310177

DOCUMENT-IDENTIFIER: US 6310177 B1

TITLE: Compounds and methods for modulating tissue permeability

DATE-ISSUED: October 30, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blaschuk; Orest W.	Westmount			CA
Symonds; James Matthew	Ottawa			CA
Gour; Barbara J.	Kemptville			CA

US-CL-CURRENT: [530/317](#); [206/569](#), [424/185.1](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 12. Document ID: US 6265549 B1

L4: Entry 12 of 29

File: USPT

Jul 24, 2001

US-PAT-NO: 6265549

DOCUMENT-IDENTIFIER: US 6265549 B1

TITLE: Methods and compositions for inhibiting endothelial cell and fibrinogen mediated inflammation

DATE-ISSUED: July 24, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Altieri; Dario C.	La Jolla	CA		
Languino; Lucia R.	La Jolla	CA		
Thornton; George B.	Ramona	CA		

US-CL-CURRENT: [530/387.9](#); [530/388.1](#), [530/389.1](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 13. Document ID: US 6248864 B1

L4: Entry 13 of 29

File: USPT

Jun 19, 2001

US-PAT-NO: 6248864

DOCUMENT-IDENTIFIER: US 6248864 B1

TITLE: Compounds and methods and modulating tissue permeability

DATE-ISSUED: June 19, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blaschuk; Orest W.	Westmount			CA
Symonds; James Matthew	Ottawa			CA
Gour; Barbara J.	Beaconsfield			CA

US-CL-CURRENT: [530/317](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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## 14. Document ID: US 6207749 B1

L4: Entry 14 of 29

File: USPT

Mar 27, 2001

US-PAT-NO: 6207749

DOCUMENT-IDENTIFIER: US 6207749 B1



TITLE: Comb copolymers for regulating cell-surface interactions

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 524/731; 427/2.1, 427/2.12, 427/2.13, 435/373, 435/374, 435/375,  
435/378, 435/402, 524/732

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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15. Document ID: US 6203788 B1

L4: Entry 15 of 29

File: USPT

Mar 20, 2001

US-PAT-NO: 6203788

DOCUMENT-IDENTIFIER: US 6203788 B1

TITLE: Compounds and methods for regulating cell adhesion

DATE-ISSUED: March 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blaschuk; Orest W.	Westmount			CA
Gour; Barbara J.	Beaconsfield			CA

US-CL-CURRENT: 424/93.7; 514/12, 514/13, 514/14, 514/15, 514/16, 514/17

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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16. Document ID: US 6150459 A

L4: Entry 16 of 29

File: USPT

Nov 21, 2000

US-PAT-NO: 6150459

DOCUMENT-IDENTIFIER: US 6150459 A

TITLE: Comb polymers for regulating cell surface interactions

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 525/54.1; 435/325, 435/395, 435/396, 435/402, 435/404, 525/165,  
525/166, 525/168, 525/54.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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17. Document ID: US 6110747 A

L4: Entry 17 of 29

File: USPT

Aug 29, 2000

US-PAT-NO: 6110747

DOCUMENT-IDENTIFIER: US 6110747 A

TITLE: Compounds and methods for modulating tissue permeability

DATE-ISSUED: August 29, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Blaschuk; Orest W.	Westmount			CA
Symonds; James Matthew	Ottawa			CA
Gour; Barbara J.	Kemptville			CA

US-CL-CURRENT: 436/512; 436/63, 436/86, 530/300, 530/317, 530/324, 530/325, 530/326,  
530/327, 530/328, 530/329, 530/330

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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18. Document ID: US 6083741 A

L4: Entry 18 of 29

File: USPT

Jul 4, 2000

US-PAT-NO: 6083741

DOCUMENT-IDENTIFIER: US 6083741 A

TITLE: Internalisation of DNA, using conjugates of poly-l-lysine and an integrin receptor ligand

DATE-ISSUED: July 4, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hart; Stephen L.	London			GB
Harbottle; Richard P.	London			GB

US-CL-CURRENT: 435/320.1; 530/317, 530/330, 530/333, 530/350, 530/378, 536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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19. Document ID: US 6051429 A

L4: Entry 19 of 29

File: USPT

Apr 18, 2000

US-PAT-NO: 6051429

DOCUMENT-IDENTIFIER: US 6051429 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Peptide-enhanced cationic lipid transfections

DATE-ISSUED: April 18, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hawley-Nelson; Pamela	Silver Spring	MD		
Lan; Jianqing	Germantown	MD		
Shih; PoJen	Columbia	MD		
Jessee; Joel A.	Mt. Airy	MD		
Schifferli; Kevin P.	Germantown	MD		
Gebeyehu; Gulilat	Silver Spring	MD		

US-CL-CURRENT: 435/458; 435/235.1, 435/320.1, 536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 20. Document ID: US 5994311 A

L4: Entry 20 of 29

File: USPT

Nov 30, 1999

US-PAT-NO: 5994311

DOCUMENT-IDENTIFIER: US 5994311 A

TITLE: Cell adhesion peptides for modifying the adhesion capacity of eukaryotic cells between each other

DATE-ISSUED: November 30, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Eichner; Wolfram	Butzbach			DE
Kock; Katharina	Friedberg			DE
Mielke; Heiko	Neu Wulmstorf			DE
Doerschner; Albrecht	Hamburg			DE

US-CL-CURRENT: 514/18; 435/371, 435/372, 435/7.21, 514/12, 514/13, 514/14, 514/15, 514/16, 514/17, 530/324, 530/325, 530/326, 530/327, 530/328, 530/329, 530/330, 530/331, 530/350, 530/356, 530/363, 530/385, 530/403

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 21. Document ID: US 5919754 A

L4: Entry 21 of 29

File: USPT

Jul 6, 1999

US-PAT-NO: 5919754

DOCUMENT-IDENTIFIER: US 5919754 A

TITLE: Method of inhibiting fibrinogen binding to endothelial cells with fibrinogen gamma chain peptides

DATE-ISSUED: July 6, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Altieri; Dario C.	La Jolla	CA		
Languino; Lucia R.	La Jolla	CA		
Thornton; George B.	Ramona	CA		

US-CL-CURRENT: 514/2; 514/12, 514/13, 514/8, 514/885, 530/324, 530/325, 530/326,  
530/382

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 22. Document ID: US 5843774 A

L4: Entry 22 of 29

File: USPT

Dec 1, 1998

US-PAT-NO: 5843774

DOCUMENT-IDENTIFIER: US 5843774 A

TITLE: Polypeptides for promoting cell attachment

DATE-ISSUED: December 1, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ginsberg; Mark H.	San Diego	CA		
Plow; Edward F.	San Diego	CA		
Bowditch; Ronald	Encinitas	CA		

US-CL-CURRENT: 435/320.1; 530/327, 536/23.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw	Draw	Image
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## 23. Document ID: US 5780426 A

L4: Entry 23 of 29

File: USPT

Jul 14, 1998

US-PAT-NO: 5780426

DOCUMENT-IDENTIFIER: US 5780426 A

TITLE: Fivemer cyclic peptide inhibitors of diseases involving .alpha..sub.v  
.beta..sub.3

DATE-ISSUED: July 14, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Palladino; Michael A.	Olivenhain	CA		
Lee; Bruce A.	San Diego	CA		
Huse; William D.	San Diego	CA		
Varner; Judith A.	Encinitas	CA		

US-CL-CURRENT: 514/9; 514/11, 514/17, 530/317, 530/329

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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## 24. Document ID: US 5773574 A

L4: Entry 24 of 29

File: USPT

Jun 30, 1998

US-PAT-NO: 5773574

DOCUMENT-IDENTIFIER: US 5773574 A

TITLE: Polypeptides for promoting cell attachment

DATE-ISSUED: June 30, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ginsberg; Mark H.	San Diego	CA		
Plow; Edward F.	San Diego	CA		
Bowditch; Ronald	Encinitas	CA		

US-CL-CURRENT: 530/327; 530/300, 530/329, 530/350, 530/395, 930/290

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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Full	Draw Desc	Image
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## 25. Document ID: US 5770565 A

L4: Entry 25 of 29

File: USPT

Jun 23, 1998

US-PAT-NO: 5770565

DOCUMENT-IDENTIFIER: US 5770565 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Peptides for reducing or inhibiting bone resorption

DATE-ISSUED: June 23, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cheng; Soan	San Diego	CA		
Ingram; Ronald	Oceanside	CA		
Mullen; Daniel	San Diego	CA		
Tschopp; Juerg	San Diego	CA		

US-CL-CURRENT: 514/11; 514/12, 514/13, 514/14, 514/15, 514/16, 514/17, 530/324, 530/325, 530/326, 530/327, 530/328, 530/329

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 26. Document ID: US 5767071 A

L4: Entry 26 of 29

File: USPT

Jun 16, 1998

US-PAT-NO: 5767071

DOCUMENT-IDENTIFIER: US 5767071 A

TITLE: Sevenmer cyclic peptide inhibitors of diseases involving .alpha..sub.v  
.beta..sub.3

DATE-ISSUED: June 16, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Palladino; Michael A.	Olivenhain	CA		
Lee; Bruce A.	San Diego	CA		
Huse; William D.	Del Mar	CA		
Varner; Judith A.	Encinitas	CA		

US-CL-CURRENT: 514/11; 514/15, 530/317, 530/328

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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27. Document ID: US 5677276 A

L4: Entry 27 of 29

File: USPT

Oct 14, 1997

US-PAT-NO: 5677276

DOCUMENT-IDENTIFIER: US 5677276 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Immobilization of peptides to hyaluronate

DATE-ISSUED: October 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dickerson; Kenneth T.	San Diego	CA		
Glass; James R.	Cardiff	CA		
Liu; Lin-Shu	Mountain View	CA		
Polarek; James W.	Del Mar	CA		
Craig; William S.	San Diego	CA		
Mullen; Daniel G.	San Diego	CA		
Cheng; Soan	San Diego	CA		

US-CL-CURRENT: 514/8; 514/13, 514/14, 514/15, 514/16, 514/17, 530/322, 530/326,  
530/327, 530/328, 530/329, 530/330, 530/345, 530/411

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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28. Document ID: US 5599790 A

L4: Entry 28 of 29

File: USPT

Feb 4, 1997

US-PAT-NO: 5599790

DOCUMENT-IDENTIFIER: US 5599790 A

TITLE: Fibrinogen .gamma. chain polypeptide and compositions thereof

DATE-ISSUED: February 4, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Altieri; Dario C.	La Jolla	CA		
Languino; Lucia R.	La Jolla	CA		
Thornton; George B.	Ramona	CA		

US-CL-CURRENT: [514/8](#); [514/13](#), [514/2](#), [530/300](#), [530/326](#), [530/382](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 29. Document ID: US 5492890 A

L4: Entry 29 of 29

File: USPT

Feb 20, 1996

US-PAT-NO: 5492890

DOCUMENT-IDENTIFIER: US 5492890 A

TITLE: Polypeptides for promoting cell attachment

DATE-ISSUED: February 20, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ginsberg; Mark H.	San Diego	CA		
Plow; Edward F.	San Diego	CA		
Bowditch; Ronald	Encinitas	CA		

US-CL-CURRENT: [514/12](#); [514/2](#), [514/21](#), [530/324](#), [530/350](#), [530/382](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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L2: Entry 1 of 16

File: PGPB

Oct 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030186323

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030186323 A1

TITLE: Force-regulated molecular recognition switches

PUBLICATION-DATE: October 2, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Vogel, Viola	Seattle	WA	US	
Krammer, Andre	Seattle	WA	US	
Schulten, Klaus	Urbana	IL	US	
Isralewitz, Barry	Urbana	IL	US	
Lu, Hui	Urbana	IL	US	

US-CL-CURRENT: [435/7.1](#); [435/287.2](#), [702/19](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachment	Claims	PMC	Draw Desc	Image
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**2. Document ID: US 20030133972 A1**

L2: Entry 2 of 16

File: PGPB

Jul 17, 2003

PGPUB-DOCUMENT-NUMBER: 20030133972

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030133972 A1

TITLE: Targeted multivalent macromolecules

PUBLICATION-DATE: July 17, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Danthi, S. Narasimhan	Mountain View	CA	US	
Bednarski, Mark David	Los Altos	CA	US	
Wartchow, Charles Aaron	San Francisco	CA	US	
Choi, Hoyul Steven	San Jose	CA	US	

US-CL-CURRENT: [424/450](#); [424/178.1](#), [530/391.1](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachment	Claims	PMC	Draw Desc	Image
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## 3. Document ID: US 20030129223 A1

L2: Entry 3 of 16

File: PGPB

Jul 10, 2003

PGPUB-DOCUMENT-NUMBER: 20030129223  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030129223 A1

TITLE: Targeted multivalent macromolecules

PUBLICATION-DATE: July 10, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Wartchow, Charles Aaron	San Francisco	CA	US	
DeChene, Neal Edward	Morgan Hill	CA	US	
Pease, John S.	Los Altos	CA	US	
Shen, Zhimin	Palo Alto	CA	US	
Trulson, Julie	San Jose	CA	US	
Bednarski, Mark David	Los Altos	CA	US	
Danthi, S. Narasimhan	Mountain View	CA	US	
Zhang, Michael	San Jose	CA	US	
Choi, Hoyul Steven	San Jose	CA	US	

US-CL-CURRENT: 424/450; 424/146.1, 424/178.1

Full	Title	Citation	Front	Reprint	Classification	Date	Reference	Sequences	Attachments
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## 4. Document ID: US 20030108587 A1

L2: Entry 4 of 16

File: PGPB

Jun 12, 2003

PGPUB-DOCUMENT-NUMBER: 20030108587  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030108587 A1

TITLE: Methods and apparatus for application of micro-mechanical forces to tissues

PUBLICATION-DATE: June 12, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Orgill, Dennis P.	Belmont	MA	US	
Eichbaum, Quentin Gavin	Watertown	MA	US	
Huang, Sui	Boston	MA	US	
Hwang, Chao-Wei	Brookline	MA	US	
Ingber, Donald E.	Boston	MA	US	
Saxena, Vishal	Cambridge	MA	US	
Garfein, Evan Stuart	Boston	MA	US	

US-CL-CURRENT: 424/423

Full	Title	Citation	Front	Reprint	Classification	Date	Reference	Sequences	Attachments
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## 5. Document ID: US 20020182241 A1

L2: Entry 5 of 16

File: PGPB

Dec 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020182241  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20020182241 A1

TITLE: Tissue engineering of three-dimensional vascularized using microfabricated polymer assembly technology

PUBLICATION-DATE: December 5, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Borenstein, Jeffrey T.	Cambridge	MA	US	
King, Kevin R.	Cambridge	MA	US	
Terai, Hidetomi	Osaka	MA	JP	
Vacanti, Joseph P.	Boston		US	

US-CL-CURRENT: 424/422; 428/188, 435/69.4, 536/56

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 6. Document ID: US 20010027237 A1

L2: Entry 6 of 16

File: PGPB

Oct 4, 2001

PGPUB-DOCUMENT-NUMBER: 20010027237  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20010027237 A1

TITLE: Comb copolymers for regulating cell-surface interactions

PUBLICATION-DATE: October 4, 2001

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Mayes, Anne M.	Waltham	MA	US	
Griffith, Linda G.	Cambridge	MA	US	
Irvine, Darrell J.	Cambridge	MA	US	
Banerjee, Pallab	Boston	MA	US	
Johnson, Terry D.	Allston	MA	US	

US-CL-CURRENT: 525/326.1; 424/422, 424/78.08, 424/78.17, 424/78.18, 525/418, 525/474

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 7. Document ID: US 6399700 B2

L2: Entry 7 of 16

File: USPT

Jun 4, 2002

US-PAT-NO: 6399700  
DOCUMENT-IDENTIFIER: US 6399700 B2

TITLE: Comb copolymers for regulating cell-surface interactions

DATE-ISSUED: June 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 524/731; 427/2.1, 427/2.12, 427/2.13, 435/325, 435/373, 435/374,  
435/375, 435/378, 435/395, 435/396, 435/402, 435/404, 524/732, 525/165, 525/166,  
525/168, 525/54.1, 525/54.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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8. Document ID: US 6207749 B1

L2: Entry 8 of 16

File: USPT

Mar 27, 2001

US-PAT-NO: 6207749

DOCUMENT-IDENTIFIER: US 6207749 B1

TITLE: Comb copolymers for regulating cell-surface interactions

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 524/731; 427/2.1, 427/2.12, 427/2.13, 435/373, 435/374, 435/375,  
435/378, 435/402, 524/732

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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9. Document ID: US 6150459 A

L2: Entry 9 of 16

File: USPT

Nov 21, 2000

US-PAT-NO: 6150459

DOCUMENT-IDENTIFIER: US 6150459 A

TITLE: Comb polymers for regulating cell surface interactions

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mayes; Anne M.	Waltham	MA		
Griffith; Linda G.	Cambridge	MA		
Irvine; Darrell J.	Cambridge	MA		
Banerjee; Pallab	Boston	MA		
Johnson; Terry D.	Allston	MA		

US-CL-CURRENT: 525/54.1; 435/325, 435/395, 435/396, 435/402, 435/404, 525/165,  
525/166, 525/168, 525/54.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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10. Document ID: US 5885829 A

L2: Entry 10 of 16

File: USPT

Mar 23, 1999

US-PAT-NO: 5885829

DOCUMENT-IDENTIFIER: US 5885829 A

**\*\* S e image for Certificate of Correction \*\***

TITLE: Engineering oral tissues

DATE-ISSUED: March 23, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mooney; David J.	Ann Arbor	MI		
Rutherford; Robert B.	Ann Arbor	MI		

US-CL-CURRENT: 435/325; 424/422, 424/435, 424/49, 435/374, 435/378, 435/69.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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11. Document ID: US 5733538 A

L2: Entry 11 of 16

File: USPT

Mar 31, 1998

US-PAT-NO: 5733538

DOCUMENT-IDENTIFIER: US 5733538 A

TITLE: Surface-modifying copolymers having cell adhesion properties

DATE-ISSUED: March 31, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Riffle; Judy S.	Blacksburg	VA		

US-CL-CURRENT: 424/78.08; 424/78.17, 424/78.18, 424/78.27, 424/78.31, 424/78.35,  
424/78.37, 514/2, 524/17, 524/188, 524/20, 524/261, 524/262, 524/265, 524/267,  
524/269, 524/498, 524/499, 524/506, 524/507, 524/515, 524/577, 524/588, 524/589,  
524/590, 525/100, 525/101, 525/102, 525/106, 525/123, 525/130, 525/217, 525/231,  
525/241, 525/452, 525/453, 525/455, 525/457, 525/54.1, 525/54.11, 525/88, 525/90,  
525/92A, 525/92C, 525/92G, 525/92R, 525/95, 525/96, 526/238.1, 526/279, 526/346,  
527/200, 527/201, 527/203, 527/204, 528/10, 528/25, 528/28, 528/44, 528/85,  
530/300, 530/345

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 12. Document ID: US 5677276 A

L2: Entry 12 of 16

File: USPT

Oct 14, 1997

US-PAT-NO: 5677276

DOCUMENT-IDENTIFIER: US 5677276 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Immobilization of peptides to hyaluronate

DATE-ISSUED: October 14, 1997

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Dickerson; Kenneth T.	San Diego	CA		
Glass; James R.	Cardiff	CA		
Liu; Lin-Shu	Mountain View	CA		
Polarek; James W.	Del Mar	CA		
Craig; William S.	San Diego	CA		
Mullen; Daniel G.	San Diego	CA		
Cheng; Soan	San Diego	CA		

US-CL-CURRENT: 514/8; 514/13, 514/14, 514/15, 514/16, 514/17, 530/322, 530/326,  
530/327, 530/328, 530/329, 530/330, 530/345, 530/411

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 13. Document ID: US 5583211 A

L2: Entry 13 of 16

File: USPT

Dec 10, 1996

US-PAT-NO: 5583211

DOCUMENT-IDENTIFIER: US 5583211 A

TITLE: Surface activated organic polymers useful for location - specific attachment of nucleic acids, peptides, proteins and oligosaccharides

DATE-ISSUED: December 10, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Coassin; Peter J.	San Juan Capistrano	CA		
Matson; Robert	Orange	CA		
Rampal; Jang	Yorba Linda	CA		

US-CL-CURRENT: 536/23.1; 435/6, 521/143, 521/53, 525/333.7, 525/340, 525/375,  
530/300, 530/350, 536/102, 536/112, 536/114, 536/123.1, 536/24.3, 536/25.3, 536/56

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 14. Document ID: US 5554501 A

L2: Entry 14 of 16

File: USPT

Sep 10, 1996

US-PAT-NO: 5554501

DOCUMENT-IDENTIFIER: US 5554501 A

TITLE: Biopolymer synthesis using surface activated biaxially oriented polypropylene

DATE-ISSUED: September 10, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Coassin; Peter J.	San Juan Capistrano	CA		
Matson; Robert S.	Orange	CA		
Rampal; Jang B.	Yorba Linda	CA		

US-CL-CURRENT: 435/6; 436/63, 436/89, 436/94, 530/334, 536/25.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 15. Document ID: US 5514581 A

L2: Entry 15 of 16

File: USPT

May 7, 1996

US-PAT-NO: 5514581

DOCUMENT-IDENTIFIER: US 5514581 A

TITLE: Functional recombinantly prepared synthetic protein polymer

DATE-ISSUED: May 7, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ferrari; Franco A.	La Jolla	CA		
Cappello; Joseph	San Diego	CA		

US-CL-CURRENT: 435/252.3; 435/252.33, 435/320.1, 536/23.4

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 16. Document ID: WO 9421386 A2 US 5686549 A WO 9421386 A3 US 5686548 A

L2: Entry 16 of 16

File: DWPI

Sep 29, 1994

DERWENT-ACC-NO: 1994-316735

DERWENT-WEEK: 199751

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TITLE: Polymers forming self-assembled, ultra thin anisotropic coatings - comprise pendant chain chemisorption bonding anchoring gp. and are useful in data disc lubrication, prosthesis treatment analysis, contact lenses and magnetic tape

INVENTOR: GRAINGER, D W; SUN, F

PRIORITY-DATA: 1993US-0037065 (March 25, 1993), 1995US-0456134 (May 31, 1995), 1995US-0456135 (May 31, 1995)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 9421386 A2	September 29, 1994		049	B05D005/00
US 5686549 A	November 11, 1997		011	C08G077/04
WO 9421386 A3	January 26, 1995		000	B05D005/00
US 5686548 A	November 11, 1997		010	C08G077/04

INT-CL (IPC): A61 F 2/00; B05 D 1/18; B05 D 5/00; C08 G 77/04; C08 G 77/38; G11 B 5/72

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REPEATABILIT	2
REPEATABILITIES	53
REPEATABILITY	16990
(RGD SAME (REPEAT\$ AND POLYMER?)).USPT,PGPB,EPAB,DWPI,TDBD.	16

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L12	0	FILE CABA
L13	0	FILE CANCERLIT
L14	2	FILE CAPLUS
L15	0	FILE CEABA-VTB
L16	0	FILE CEN
L17	0	FILE CIN
L18	0	FILE CONFSCI
L19	0	FILE CROPB
L20	0	FILE CROPU
L21	0	FILE DISSABS
L22	8	FILE DGENE
L23	0	FILE DRUGB
L24	0	FILE DRUGLAUNCH
L25	0	FILE DRUGMONOG2
L26	0	FILE DRUGNL
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L107 ANSWER 1 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-10988 BIOTECHDS

TITLE: Inhibiting amyloid toxicity or the formation of an amyloid  
deposit, comprises administering an agent that binds to an  
integrin, integrin subunit, or laminin;  
amyloid toxicity inhibition and sense and antisense  
sequence for use in gene therapy

AUTHOR: PRENNER I G; WRIGHT S; YEDNOCK T; RYDEL R

PATENT ASSIGNEE: ELAN PHARM INC

PATENT INFO: WO 2003006893 23 Jan 2003

APPLICATION INFO: WO 2002-US19803 8 Jul 2002

PRIORITY INFO: US 2001-341772 17 Dec 2001; US 2001-304315 9 Jul 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-221770 [21]

AN 2003-10988 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Inhibiting amyloid toxicity or the formation of an amyloid  
deposit, comprising administering a dosage of one or more agent(s) that  
bind(s) to a molecule selected from an integrin subunit such as alpha2,  
alphav, alpha6 or beta1, an integrin such as alpha2beta1, alpha6beta1 or  
alphavbeta1, and laminin, under conditions such that the agent(s) inhibit  
amyloid toxicity or the formation of an amyloid deposit, is new.

BIOTECHNOLOGY - Preferred Method: In the method, the effective  
dosages of at least 2 (preferably at least 4) agents that bind to the  
integrin subunits are administered to a patient. The agent is a peptide  
comprising an **RGD** (Arg-Gly-Asp) **motif**, a ligand of  
the integrins cited above, or fibronectin or superfibronectin. The agent  
inhibits adhesion of alpha2 integrin subunit-expressing cells to  
collagen. The agent also inhibits adhesion of alphav integrin  
subunit-expressing cells to osteopontin, or vitronectin or fibronectin;  
adhesion of beta1 integrin subunit-expressing cells to fibronectin; or  
adhesion of alpha6 integrin subunit-expressing cells to osteopontin. In  
addition, the agent is a monoclonal or polyclonal antibody selected from  
1965, Lia1/2, Gi9, 1950Z, VNR147 and 1980, or that recognizes the same  
epitope as an antibody selected from 1965, Lia1/2, Gi9, 1950Z, VNR147 and  
1980. The agent competes for binding to the integrin alpha2beta1 or  
alphavbeta1 with the antibody cited above. The agent is a human antibody,  
a humanized antibody, a mouse antibody, or an antibody fragment. It  
comprises one or more heavy chains, light chains, F(ab), F(ab)2, F(ab)c,  
or F(v) of an antibody. The isotype of the antibody is immunoglobulin  
(Ig)1, Ig2, Ig3 or Ig4. The agent is an antibody chain and it comprises 2  
pairs of light and heavy chains. The agent is administered with a carrier  
as a **pharmaceutical composition**. The patient is  
suffering from an amyloidogenic disease, such as Alzheimer's disease,  
type II diabetes, Parkinson's disease, a disease caused all or in part by  
prion infection, hereditary or systemic amyloidosis, or Down's syndrome.

A nucleic acid is administered that encodes the agent, where the agent is an antisense RNA molecule, an antisense DNA molecule, a ribozyme, RNAi, or a zinc-finger protein.

ACTIVITY - Nootropic; Neuroprotective; Antidiabetic; Antiparkinsonian. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The method is useful for inhibiting amyloidogenic protein toxicity, inhibiting the formation of an amyloidogenic protein deposit and/or treating amyloidogenic diseases, such as Alzheimer's disease, type II diabetes, Parkinson's disease, a disease caused all or in part by prion infection, hereditary or systemic amyloidosis, or Down's syndrome.

ADMINISTRATION - The dosage of the antibody is 0.01-10 mg/kg of body weight (claimed). The agent is administered intraperitoneally, orally, intranasally, subcutaneously, intrathecally, intramuscularly, topically or intravenously (claimed).

EXAMPLE - No suitable example given. (43 pages)

L107 ANSWER 2 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-02772 BIOTECHDS

TITLE: New modified fusion protein with reduced immunogenicity, useful for combining favorable properties of a composition, comprises an immunoglobulin molecule linked to a non-immunoglobulin target polypeptide; recombinant fusion protein production useful for disease therapy

AUTHOR: GILLIES S; CARR F J; JONES T; CARTER G; HAMILTON A; WILLIAMS S; HANLON M; WATKINS J; BAKER M; WAY J C

PATENT ASSIGNEE: MERCK PATENT GMBH

PATENT INFO: WO 2002066514 29 Aug 2002

APPLICATION INFO: WO 2002-EP1690 18 Feb 2002

PRIORITY INFO: EP 2001-108291 5 Apr 2001; EP 2001-103955 19 Feb 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-667054 [71]

AN 2003-02772 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - An immunogenically modified fusion protein (I) derived from a parent fusion protein, comprising first and second proteins/polypeptides, where the first protein is an immunoglobulin molecule or its fragment and the second protein is non-immunoglobulin target polypeptide each linked to the other directly or by a linker molecule, is new.

DETAILED DESCRIPTION - An immunogenically modified fusion protein (I) derived from a parent fusion protein, comprises first and second proteins/polypeptides, where the first protein is an immunoglobulin molecule or its fragment and the second protein is non-immunoglobulin target polypeptide each linked to the other directly or by a linker molecule. (I) also comprises an amino acid sequence different from that of the parent fusion protein and exhibits reduced immunogenicity by a reduced number of T-cell epitopes within its amino acid sequence relative to the parent fusion protein when exposed to the immune system of a given species. INDEPENDENT CLAIMS are also included for the following: (1) a DNA sequence encoding the fusion protein; (2) an expression vector comprising the above DNA sequence; (3) a **pharmaceutical composition** comprising (I) and optionally, a carrier, excipient or diluent; (4) preparing (I), comprising: (a) determining the amino acid sequence of the parent fusion protein or its part; (b) identifying one or more potential T-cell epitopes within the amino acid sequence of the fusion protein by any method including determination of the binding of the peptides to Major Histocompatibility Complex (MHC) molecules using in vitro or in silico techniques or biological assays; (c) designing new sequence variants by alteration of at least one amino acid residue within the originally identified T-cell epitope sequences, where the variants are modified in such a way to substantially reduce or eliminate the activity or number of the T-cell epitope sequences and/or the number of MHC allotypes able to bind peptides derived from the biological molecule as determined by the binding of the peptides to MHC molecules using in



vitro or in silico techniques or biological assays or by binding of peptide-MHC complexes to T-cells; (d) constructing sequence variants by recombinant DNA techniques and testing the variants to identify one or more variants with desirable properties; and (e) optionally repeating steps (b) - (d), characterized in that the identification of T-cell epitope sequences according to step (b) is achieved by: (i) selecting a region of the peptide having a known amino acid residue sequence; (ii) sequentially sampling overlapping amino acid residue segments of predetermined uniform size and constituted by at least three amino acid residues from the selected region; (iii) calculating MHC Class II molecule binding score for each sampled segment by summing assigned values for each hydrophobic amino acid residue side chain present in the sampled amino acid residue segment; and (iv) identifying at least one of the segments suitable for modification based on the calculated MHC Class II molecule binding score for that segment, to change overall MHC Class II binding score for the peptide without substantially reducing therapeutic utility of the peptide; and (5) an immunogenically modified artificial protein comprising Y-(L)-X, P-(L)-X, or A-(L)-X derived from a parent artificial protein having an amino acid sequence which is different from that of the parent artificial protein and exhibits reduced immunogenicity by a reduced number of T-cell epitopes relative to the parent fusion protein when exposed to the immune system of a given species, where T-cell epitopes are peptide sequences able to bind to MHC class II molecule binding groups obtained by method (4). Y = cytokine; L = linker peptide; P = a protein with unusual glycosylation moieties; A = an immunoglobulin or its fragment; and X = non-immunoglobulin target polypeptide.

**BIOTECHNOLOGY - Preferred Fusion Protein:** The T-cell epitopes are peptide sequences able to bind to MCH class II molecule binding groups. The target polypeptide is linked by its N-terminal to the C-terminal of the immunoglobulin moiety. The given species cited above is a human. The fusion components are fused via a linker molecule L which is non-immunogenic or less immunogenic. The fusion region represented the C-terminal region of the immunoglobulin portion and the N-terminal region of the non-immunoglobulin target polypeptide which has no or a reduced number of T-cell epitopes. The immunoglobulin portion, or its fragment, and the target polypeptide are less immunogenic. The immunoglobulin molecule or its fragment is IgG1 or IgG2. The fragment comprises the Fc portion which has a reduced affinity to Fc receptors. The modified fusion protein comprises the formula: Fc-Ln-X Fc = portion of an immunoglobulin molecule (antibody); n = 0 or 1; and X or L = a molecule as defined above; where X and/or L comprise(s) amino acid residue modifications which elicit a reduced immunogenicity compared to the parent molecule. Additionally, the fusion protein comprises a modified molecule, where the fusion region between the Fc and X and, optionally, Fc and L and/or L and X, has no or a reduced number of T-cell epitopes. The modified fusion protein may also comprise the formula A-Ln-X A = a whole antibody or its sFv, Fab, Fab' or F(ab')<sub>2</sub> fragments; and X, L, and n = as defined above; where A and/or X and/or L comprise(s) amino acid residue modifications which elicit a reduced immunogenicity compared to the parent molecule. Furthermore, the fusion region between A and X and optionally A and L and/or L and X has no or a reduced immunogenicity. A is selected from anti-EGF receptor (HER1) antibodies, anti-HER2 antibodies, anti-CDx antibodies, anti-cytokine receptor antibodies, anti-17-1A antibodies, anti-KSA antibodies, anti-GP IIb/IIIa antibodies, anti-integrin receptor antibodies and anti-VEGF receptor antibodies. The antibody is selected from monoclonal antibody 225, monoclonal antibody 425, monoclonal antibody KS 1/4, monoclonal antibody 14.18, monoclonal antibody 4D5/HER2 Herceptin (RTM), monoclonal antibody 17-1A, monoclonal antibody 7E3, monoclonal antibodies LM609, P1F6 and 14D9.F8, monoclonal antibody DC-101 and monoclonal anti-I1-2R antibody Zenapax (RTM) and their derivatives. The target polypeptide is selected from cytokines, integrin inhibitors, soluble cytokine receptors, glycoproteins, hormones, glycoprotein hormones, leptin, growth hormones, growth factors, anti-hemophilic factors, antigens, and cytokine receptor antagonists. Alternatively, the target polypeptide is selected from IL-2, G-CSF,

GM-CSF, EPO, TPO, TNFalpha, soluble TNF receptor, IL-12, IL-8, FGF, TGF, EGF, VEGF, PMSA, IGF, insulin, hGH, RGD-peptides, endostatin, angiostatin, BDNF, CNTF, protein c, factor IX, and their biological ly active fragments. The modified fusion protein is selected from MAb KS 1/4-IL2, MAb 14.18-IL2, MAb 425-IL2, MAb c425-IL2, MAb h425-IL2, MAb 425-TNFa, MAb 225-IL2, MAb c225-IL2, MAb 4D5-IL2, MAb DC101-I12, MAb LM609-IL2, Fc-IL2, Fc-TNFa, Fc-G-CSF, Fc-EPO, Fc-Leptin, Fc-KGF, Fc-BDNF, Fc-CNTF, FC-beta-Cerebrosidase, Fc-TPO, and Fc-GM-CSF. The immunogenically modified artificial protein prefers that at least A or X or Y or P is immunogenically modified. Preferred DNA Sequence: The DNA sequence comprises: (a) a signal sequence; (b) a DNA sequence encoding all domains or Fc, sFV, Fab, Fab' or F(ab')<sub>2</sub> domain of an IgG1, IgG2 or IgG3 antibody; (c) a DNA sequence encoding the polypeptide (X); and optionally (d) a DNA sequence encoding the linker molecule. Preferred Method: In preparing the modified fusion protein, step (iii) is carried out by using a Bohm scoring function modified to include 12-6 van der Waal's ligand-protein energy repulsive term and ligand conformational energy term by: (a) providing a first data base of MHC Class II molecule models; (b) providing a second database of allowed peptide backbones for the MHC Class II molecule models; (c) selecting a model from the first database; (d) selecting an allowed peptide backbone from the second database; (e) identifying amino acid residue side chains present in each sampled segment; (f) determining the binding affinity value for all side chains present in each sampled segment; and optionally (g) **rep ating** steps (a)-(e) for each model and backbone. The sampled amino acid residue segment is constituted by 13 amino acid residues. Consecutive sampled amino acid residue segments overlap by one to five amino acid residues. Amino acid residues 1-9 of the originally present T-cell epitope sequences are altered, preferably, one amino acid residue in any of the originally present T-cell epitope sequences is altered. The alteration of the amino acid residues is substitution, deletion or addition of originally present amino acid(s) residue(s) by other amino acid residue(s) at specific position(s). Additionally, alteration by substitution, deletion or addition is conducted to restore biological activity of the biological molecule.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - The immunogenically modified fusion protein is useful in combining known favorable properties of a composition or in creating new properties of a composition which elicits biological or pharmacological efficacy without having undesirable physiological effects such as nausea or gastric upset. The method is useful in preparing the fusion proteins.

ADMINISTRATION - The composition may be given at a dose of 10-1000 (preferably 50-100) mg/kg of body weight per day. The antibody can be given at 0.1-300 (preferably 0.5-20) mg/kg in one or more dose administrations daily for one or several days. No administration details given.

EXAMPLE - No suitable example is given. (92 pages)

L107 ANSWER 3 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-02235 BIOTECHDS

TITLE: New product comprising a dendroaspin scaffold and a serine protease inhibitor domain ligated to the dendroaspin scaffold, useful for treating or preventing diseases associated with thrombosis, e.g. myocardial infarction, stroke;  
dendroaspin scaffold, serine protease-inhibitor domain and vector expression in host cell use in disease therapy and drug screening

AUTHOR: LU X; KAKKAR V V

PATENT ASSIGNEE: TRIGEN LTD

PATENT INFO: WO 2002063017 15 Aug 2002

APPLICATION INFO: WO 2002-GB500 5 Feb 2002

PRIORITY INFO: US 2001-267234 5 Feb 2001; US 2001-267234 5 Feb 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-643417 [69]

AN 2003-02235 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A product comprising a dendroaspin scaffold and a second portion comprising a serine protease inhibitor domain ligated to the dendroaspin scaffold, is new. The dendroaspin scaffold optionally has the native **RGD motif** deleted or replaced. The amino acid sequence has no integrin-binding activity or an integrin-binding amino acid sequence, and comprises a tripeptide sequence other than **RGD** containing D or E adjacent to G.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a polyamino acid comprising a nematode anticoagulant protein (NAP)-based domain having serine protease inhibitor activity linked through a proline-containing domain to another domain having integrin binding activity; (2) a hybrid polyamino acid comprising two domains, not derived from the same native molecule, interlinked by a linker comprising an imino acid residue; (3) a nucleic acid molecule encoding the polypeptide product cited above; (4) a plasmid comprising the nucleic acid in (3); (5) plasmid pGEX-3X comprising the nucleic acid in (3); (6) a host cell transformed with the plasmid in (5); (7) a cell culture comprising the host cell in (6); (8) producing the novel polypeptide product, comprising culturing the host cell in (6) to express the polypeptide, extracting the polypeptide from the culture and purifying it; (9) producing a polypeptide comprising an integrin-binding protein, or its homolog; (10) a polypeptide product obtainable by the methods of (8) or (9); (11) a **pharmaceutical composition** comprising any of the polypeptide products; (12) treatment or prophylaxis of a disease associated with thrombosis in a human or animal patient, comprising administering to the patient an effective amount of the pharmacologically active product; (13) a linker comprising an amino acid sequence selected from Aal-Gly and Gly-Aal, where Aal is an imino acid; (14) a linker which comprises at least two non-adjacent imino acids; and (15) a product comprising first and second biologically active moieties linked through the linker.

BIOTECHNOLOGY - Preferred Product: The product comprises a second portion that is ligated to the N-terminus of the dendroaspin scaffold. The first portion, which is an integrin-binding protein, a homologue having a binding activity, or their fragment, has a binding activity. A second portion is ligated to the first portion, which has a different function. The different function is a serine protease inhibitor function. The homolog has at least 50, 65, 75, or 85 % amino acid sequence homology with the wild-type protein. The wild-type protein comprises an-integrin-binding sequence, which is **RGD** or **KGD**. The homologue contains, in place of its native integrin-binding sequence, another integrin-binding sequence comprising a tripeptide sequence containing D or E adjacent to G. The second portion comprises a protein or a polypeptide having a wild type sequence. The protein or polypeptide of the second portion has a sequence that is a modification of a wild-type sequence. The protein or polypeptide has a degree of homology with its wild-type protein, which is at least 50, preferably at least 85%. The protein or polypeptide of the second portion comprises a tick anticoagulant protein (TAP) protein, a NAP protein or an AcAP protein or their homologues, having factor Xa inhibitor function. The protein or polypeptide preferably comprises NAP5 or its homologue, having factor Xa inhibitor function. The second portion comprises a fragment of a protein or polypeptide cited above. The ligation of the second portion is through a linker. The linker comprises a polyamino acid, which comprises at least one imino acid residue. The polyamino acid has 5-20 or 2-5 amino acid residues. The linker comprises at least a pair of non-adjacent imino acid residues. A glycine is adjacent to each imino acid residue. The linker comprises a region of at least 5 amino acid residues consisting solely of glycine and imino acid residues and having the sequence GPGP(G)nPG, where n = 1-10. The number of amino acid residues in the region cited above is from 5-20. The imino acid is preferably proline. The linker further comprises a PGP sequence. The protein comprised in the second portion is a snake venom protein and optionally is a disintegrin, applaggin,

kistrin, echstatin, fiavoridin, albolabrin, decorsin or dendroaspin. The tripeptide sequence has the formula: B-J-Z, J-Z = GD or GE; B = R, K, O, A, H, N, A, V, I, L, M, F, P or W; B-J = DG or EG; Z = any amino acid; J = D or E; and B and Z = each independently selected from A, V, I, L, M, F, P or W. B can preferably be R, K, Q, A, H or N; or R, K, Q or A. B-J-Z is bonded at its C-terminal end to M, W, N or V. The M, W, N or V residue is followed by the P, which is a position 47 of wild type dendroaspin, or by an A residue. The snake venom protein cited above is dendroaspin and the integrin-binding amino acid sequence is preceded by the P which is at position 42 of wild type dendroaspin or by an A residue. B can A, V, I, M, F, P, W, preferably L or V. B is L and is preceded by M. Z can be E, R or P. The snake venom protein can be dendroaspin and Z is followed by the P which is at position 47 of wild type dendroaspin, or by an A inserted before the wild type position 47 P. B-J-Z can preferably be LDV and can be preceded by an I residue. The product comprises a replacement amino acid sequence having no integrin binding activity. The replacement amino acid sequence has a receptor binding function. The binding activity is receptor-binding activity. The replacement amino acid sequence, in its native polypeptide, enters a pocket to function. The product also comprises a sequence having the binding activity, which in its native polypeptide, enters a pocket to function. The dendroaspin snake venom protein comprises the amino acids flanking RGD or the integrin binding sequence, which are modified as compared with wild-type dendroaspin. The product contains not more than 100 amino acid residues more than the native dendroaspin, or the native snake venom protein. The dendroaspin scaffold has GPIIb/IIIa binding function. The second portion is a TAP protein, a NAP protein or an AcAP protein, their homologue or fragment, and has Factor Xa inhibitor function. The dendroaspin scaffold is ligated at its N-terminus to the second portion through a linker comprising a region consisting solely of glycine and proline residues. The second portion comprises residues 1-40 of a 112 residue amino acid sequence (ND9-F3), given in the specification or its homolog, or residues 8-84 of a 156 amino acid sequence (ND9-F1), given in the specification. The dendroaspin scaffold has an **RGD motif** in loop III. The non-RGD residues of loop III are unmodified as compared with native dendroaspin or are modified by substitution, insertion and/or deletion of 1, 2 or 3 amino acid residues. The non-RGD residues are unmodified or modified by substitution of 1, 2 or 3 amino acid residues. Loop III has the sequence of loop III of ND9-F1 on residues 93-103. Loop III can also have the sequence of loop III of native dendroaspin on residues 40-50 of a 59 amino acid sequence, given in the specification. The dendroaspin scaffold outside loop III is unmodified as compared with dendroaspin or is modified by substitution, insertion and/or deletion of from 1-10 residues, or residues 1, 2, or 3. The dendroaspin scaffold has the sequence of native dendroaspin or the sequence of residues 54-112 ND9-F3. The product in (16) comprises protein as moiety. Preferred Polyamino Acid: The polyamino acid comprises other domain, which has a dendroaspin sequence. The hybrid polyamino acid comprises a linker having at least two non-adjacent imino acid residues. 67. The linker contains from 2 to 5 imino acid residues. The non-adjacent imino acid residues comprise a pair of imino acid residues separated by 1-10 amino acid residues. At least one imino acid is adjacent a glycine residue. The linker comprises at least two non-adjacent imino acid residues, which are adjacent a glycine residue. The linker comprises a sequence: IA-(G)n-IA, IA = is an imino acid; G = glycine; and n = 1-10. The linker can also comprise the sequence IA-G-IA, or G-IA-G-IA-G(n)-IA-g. Each imino acid is proline. One of the two domains has platelet binding activity and the other of the two domains has an activity selected platelet binding activity, anticoagulant activity, antithrombotic activity, inhibition of cell migration, inhibition of cell proliferation, inhibition of a component in the clotting cascade and regulation of signal transduction. One of the two domains confers GPIIb/IIIa binding activity and the other of the two domains confers platelet derived growth factor (PDGF) activity, glycoprotein IBalpha activity, hirudin activity, thrombomodulin activity, vascular epidermal growth factor activity, transforming growth factor-beta1 activity, basic

fibroblast growth factor activity, angiotensin II activity, factor VIII activity, von Willebrand factor activity, TAP activity or NAP activity. The other of the two domains comprises a sequence derived from PDGF, glycoprotein IB $\alpha$ , hirudin, thrombomodulin, vascular epidermal growth factor, transforming growth factor- $\beta$ 1, basic fibroblast growth factor, angiotensin II, factor VIII, von Willebrand factor, TAP or NAP, or a sequence having homology to any of their parts. Preferred Nucleic Acid: The nucleic acid molecule is operatively linked to a promoter and optionally to a nucleic acid sequence encoding a heterologous protein or peptide to encode a fusion product. The promoter is IPTG inducible and optionally the heterologous protein or peptide is glutathione S-transferase. Preferred Host Cell: The host cell is preferably Escherichia coli. Preferred Method: Producing a polypeptide comprising an integrin-binding protein, or its homolog comprises: (a) preparing an expression vector comprising a nucleic acid sequence encoding a polypeptide product operatively linked to a promoter and optionally linked to a nucleic acid sequence encoding a heterologous affinity purification protein for co-expression, further comprises: (a) assembling from overlapping oligonucleotides the coding sequence of an integrin-binding protein or its homologue having a binding activity; (b) assembling from overlapping oligonucleotides the coding sequence of the second portion; (c) amplifying the coding sequences, the PCR primers being designed to allow cloning of the integrin-binding protein and the second portion into an expression vector, the PCR primers optionally encoding a linker to interlink the integrin-binding protein and the second portion; and (d) preparing an expression vector comprising the coding sequences operatively linked to a promoter and optionally linked to a nucleic acid sequence encoding a heterologous affinity purification protein for co-expression; and (b) transforming a host cell with the vector and causing the host cell to express the nucleic acid sequence. The method further comprises modifying the nucleic acid sequence of the vector by one or more of the insertion, deletion or substitution of nucleic acid residues. Step (a) further comprises constructing from oligonucleotides an expression vector comprising a nucleic acid sequence encoding a dendroaspin sequence in which the RGD-encoding domain has been deleted or replaced by a replacement amino acid sequence and, optionally, modifying at least one other domain of the nucleic acid sequence of the vector encoding the dendroaspin scaffold by one or more of insertion, deletion or substitution of nucleic acid residues so that on expression, the dendroaspin scaffold comprises a corresponding domain having a non-wild-type dendroaspin sequence. The method further comprises extracting the expressed polypeptide from a host cell culture, and purifying the polypeptide from the cell culture extract. If the polypeptide is a fusion protein with a heterologous affinity purification protein, the method further comprises cleaving the desired product from the heterologous affinity purification portion of the fusion protein. The heterologous affinity purification protein is glutathione S-transferase (GST) and the purification involves GST affinity chromatography followed by the cleavage of the modified dendroaspin from GST. Preferred Composition: The **pharmaceutical composition** further comprises an excipient or a carrier. Preferred Linker: The linker comprises the amino acid sequence contained in Aa1-Gly-Aa2, where Aa1 and Aa2 = imino acids, preferably proline. The sequence can also be contained in the amino acid sequence GlyAa1-Gly-Aa2-Gly. The sequence contains 5-20 amino acids.

ACTIVITY - Thrombolytic; Cardiant; Cerebroprotective. No biological data is given.

MECHANISM OF ACTION - Serine protease inhibitor; Factor Xa inhibitor.

USE - The product is useful for the manufacture of a medicament for the treatment or prophylaxis of diseases associated with thrombosis, e.g. thrombosis, myocardial infarction, retinal neovascularization, endothelial injury (claimed), stroke, pulmonary embolism.

ADMINISTRATION - Dosage is 0.001-100 (preferably 0.02-15) mg/kg at peroral administration and 0.001-50 mg/kg at parenteral administration. The products can be administered via the oral, intravenous, subcutaneous,

intraperitoneal, intrasternal, intraarticular, buccal, rectal, dermal, nasal, tracheal, or bronchial routes.

ADVANTAGE - The invention provides compounds that are orally active and have rapid onset of activity and low toxicity as compared to various agents for preventing blood clots, e.g. aspirin, dipyridamole and filopidine, which have a potential side effect of causing prolonged bleeding.

EXAMPLE - A synthetic dendroaspin gene was constructed by ligating 10 complementary and overlapping oligonucleotides coding for the protein sequence of dendroaspin, using Escherichia coli codon usage data and cloned into plasmid pGEX-3X. The recombinant dendroaspins were purified by suspending the cell pellets in phosphate buffered saline (PBS) buffer containing 1% Triton X-100 and protease inhibitors PMSF (undefined), pepstatin, aprotinin, trypsin inhibitor, 1 mM ethylenediaminetetraacetic acid (EDTA), and sonicated on ice. The sonicated mixture was centrifuged at 7800 x g at 4 degrees C to pellet the cell debris and insoluble material. Recombinant glutathione-S-transferase (GST)-dendroaspin and GST-mutant dendroaspins from supernatants were purified by affinity chromatography on glutathione-Sepharose CL-4B columns by absorption in PBS containing 150 mM NaCl and elution with 50 mM Tris-HCl containing 10 mM reduced glutathione (pH 8.0). Purified wild-type dendroaspin and mutants were characterized by 20 % sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and electrospray ionization mass spectrometry. (68 pages)

L107 ANSWER 4 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2003-00448 BIOTECHDS

TITLE: New adeno-associated virus vector comprises a biotinylated capsid or capsid protein with an amino acid insertion in the VP1 capsid, useful as a vaccine or for transferring a therapeutic peptide to a cancer cell;  
vector-mediated gene transfer and expression in host cell for nucleic acid vaccine and gene therapy

AUTHOR: BARTLETT J S

PATENT ASSIGNEE: CHILDRENS HOSPITAL INC

PATENT INFO: WO 2002053703 11 Jul 2002

APPLICATION INFO: WO 2002-US152 4 Jan 2002

PRIORITY INFO: US 2001-260124 5 Jan 2001; US 2001-260124 5 Jan 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-583608 [62]

AN 2003-00448 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Adeno-associated virus (AAV) vector (I) comprising a biotinylated capsid or capsid protein (II) with an amino acid insertion following the capsid amino acid at position 139, 161, 588 or 657 in the VP1 capsid consisting of a fully defined sequence of 735 amino acids given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a polynucleotide (III) encoding (II); (2) a cell transfected with (III); (3) producing (M1) (I) with a capsid protein with an amino acid insertion, by growing a packaging cell and providing the packaging cell with helper virus functions, where the packaging cell comprises (III), the AAV rep gene and a recombinant AAV genome comprising deoxyribonucleic acid (DNA) of interest flanked by AAV inverted terminal **repeats**; (4) transferring (M2) a DNA of interest to a cell by delivering to the cell: (a) an AAV vector; or (b) an AAV vector encoding the DNA of interest to the cell, where the AAV vector comprises a capsid protein containing one or more amino acid insertions that ablate the ability of the vector to bind heparin-sulfate proteoglycan and allow the vector to use a cellular receptor not used by wild type AAV for DNA transfer; (5) a **pharmaceutical composition** comprising (I); (6) an immunogenic composition (IV) comprising (I); (7) eliciting (M3) an immune response in an animal by administering (IV); and (8) infecting (M4) a cell by administering to the cell an AAV vector comprising a capsid protein containing one or more amino acid insertions that ablate the

ability of the vector to bind heparin-sulfate proteoglycan and allow the vector to use a cellular receptor not used by wild type AAV for infection.

BIOTECHNOLOGY - Preferred Vector: The position may correspond to position 139, 161, 459, or 584. The amino acid insertion comprises a targeting peptide: (A) Cys-Asp-Cys-Arg-Gly-Asp-Cys-Phe-Cys; (B) Thr-Pro-Pro-Tyr-Leu-Lys; and (C) His-Cys-Ser-Thr-Cys-Tyr-Tyr-His-Lys-Ser. The amino acid insertion may also comprise an immunogen, a substrate for an enzymatic reaction, which is a biotin acceptor peptide with the sequence Gly-Leu-Asn-Asp-Ile-Phe-Glu-Ala-Gln-Lys-Ile-Glu-Trp-His-Glu. The amino acid insertion is flanked by a linker/scaffolding sequence selected from: (A) amino acids Thr-Gly amino terminal to the insertion and Ala-Leu-Ser carboxy terminal to the insertion; (B) amino acids Thr-Gly amino terminal to the insertion, and Leu-Leu-Ala carboxy terminal to the insertion; and (C) amino acids Thr-Gly amino terminal to the insertion and Gly-Leu-Ser carboxy terminal to the insertion. The AAV vector is preferably an AAV2 vector. Preferred Method: In (M1) the cell expresses a biotin ligase. (M1) also comprises treating (I) produced with biotin ligase. In transferring a DNA to a cell, the cell is a cancer cell, particularly an ovarian cancer cell, where the DNA encodes a therapeutic peptide or a reporter peptide, or is an antisense nucleic acid or ribozyme. In infecting a cell, (I) infects the cell at a titer comparable to wild type AAV vector.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - Modified (I) are useful as vaccines to elicit immune responses to amino acids, where the response can be protective and/or therapeutic. (I) may be used to transfer a therapeutic peptide to a cancer cell, particularly to an ovarian cancer cell.

EXAMPLE - Regions of the adeno-associated virus (AAV) 2 capsid deoxyribonucleic acid (DNA) to be modified were chosen by analyzing data from a number of sources to predict which encoded capsid amino acids that were exposed on the surface of the virion and which encoded amino acids that could be replaced with other amino acids without significantly altering the conformation of the rest of the capsid protein. A source of data was a comparison of structural information from 5 related autonomous parvoviruses. The AAV2 capsid primary amino acid sequence was compared with that of other AAV and other parvoviridae for regions of defined secondary structure to create a model of the AAV2 capsid. Sites for insertion of small peptides 2-15 amino acids in length were chosen. A series of 38 virus mutants containing peptide insertions at 25 unique sites within the AAV2 capsid protein was generated. Most of the insertions were within the VP1 capsid protein, 4 within the VP1 unique region, and 2 were within the VP1/VP2 unique region. Site directed mutagenesis was performed on plasmid pUC-Cap, and was confirmed by restriction endonuclease digestion. Altered Cap genes were substituted of the wild type AAV2 sequences in plasmid pACG2 to generate the series of mutant helper plasmids, where epitope AgeI is the amino acid encoded by an AgeI restriction site, epitope NgoMI is the amino acid encoded by an NgoMI restriction site, epitope 4C-RGD is a cyclic RGD-based peptide (Cys-Asp-Cys-Arg-Gly-Asp-Cys-Phe-Cys) that has been shown to bind a number of integrins present on the surface of mammalian cells that is useful for targeting tumor endothelium and other cell types, epitope BPV is a peptide from bovine papilloma virus (Thr-Pro-Pro-Tyr-Leu-Lys) and epitope LH is a receptor-binding peptide from leutenizing hormone (His-Cys-Ser-Thr-Cys-Tyr-Tyr-His-Lys-Ser). (57 pages)

L107 ANSWER 5 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-19988 BIOTECHDS

TITLE: Chimeric molecule useful in situ and in vivo imaging of cells and tissues e.g. tumor tissues comprises a first domain and a second domain;

recombinant protein production via plasmid expression in host cell for use in disease therapy and drug screening

AUTHOR: CHINNAIYAN A M; REHEMTULLA A; ROSS B D

PATENT ASSIGNEE: UNIV MICHIGAN

PATENT INFO: WO 2002047537 20 Jun 2002  
APPLICATION INFO: WO 2000-US48157 11 Dec 2000  
PRIORITY INFO: US 2000-734628 11 Dec 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-547820 [58]  
AN 2002-19988 BIOTECHDS  
AB DERWENT ABSTRACT:

NOVELTY - A chimeric molecule (I) comprising a first domain and a second domain, the first domain comprising one of a group (A) and the second domain comprising one of a group (B), is new.

DETAILED DESCRIPTION - A chimeric molecule (I) comprising a first domain and a second domain, the first domain comprising one of a group (A) and the second domain comprising one of a group (B), is new. The first domain comprises (A), which is a fluorescent (b1), bioluminescent (b2) or chemiluminescent (b3) polypeptide, or a heterologous kinase, the second domain comprises a member (B) which is an **RGD motif**-comprising polypeptide, a selectin-binding polypeptide, a matrix metalloproteinase (MMP)-binding polypeptide or a chondroitin sulfate proteoglycan-binding polypeptide. INDEPENDENT CLAIMS are included for the following: (1) a gold nanoparticle (II) comprising (I); (2) a pharmaceutical formulation (III) comprising (I) and an excipient, the formulation being suitable for administration as an imaging enhancing agent; (3) a pharmaceutical formulation (IV) comprising a composition (C) comprising a first domain comprising an imaging enhancing agent (a1) and a second domain comprising a polypeptide that binds to a cell, a tissue or an organ in a cell-, tissue-, or organ-specific manner, and an excipient. (C) is not an antibody; (4) a nucleic acid (V) encoding (I); (5) a nucleic acid (VI) comprising an open reading frame operably linked to a promoter, the open reading frame encodes (I); (6) an expression vector (VII) or a cell comprising (V); (7) a recombinant chimeric polypeptide (VIII) produced by a cell comprising (V); (8) in situ or in vivo imaging (M1) of a cell, a tissue, an organ or a full body comprising either: (a) administration of (III) to enhance the image generated by computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), bioluminescence imaging (BLI) or its equivalent; or (b) administering (III) to the human to generate the cell, tissue or body image and imaging the distribution of (III) with an imaging device, the imaging device is a CAT, MRS, MRI, PET, SPECT or BLI device or its equivalent; (9) in vivo imaging (M2) a tumor neovasculature in an individual involving administering (III) to the tumor neovasculature to generate the cell, tissue or body image and imaging the distribution of (III) with an imaging device; and (10) in vivo (M3) screening for an anti-tumor agent by imaging the tumor neovasculature in the individual involving administering a composition comprising (I) or (III) to image the tumor neovasculature and imaging the distribution of either of the compositions with the imaging device, administering the test compound and imaging the distribution of the composition with the imaging device, therefore imaging the tumor neovasculature, where decrease in the amount of tumor neovasculature indicates that the compound is an anti-tumor or an anti-angiogenic agent.

WIDER DISCLOSURE - Disclosed is a kit comprising the composition (preferably the **pharmaceutical composition**, nucleic acid or cells) and instructional material teaching methodologies.

ACTIVITY - None given.

MECHANISM OF ACTION - None given. No suitable data given.

USE - (I) is useful in gold nanoparticles and as an imaging enhancing agent in a **pharmaceutical composition**, in a nucleic acid, an expression vector and in a cell which is useful for producing a recombinant chimeric polypeptide, in situ or in vivo imaging of a cell, a tissue, an organ or a full body, in vivo imaging a tumor neovasculature in an individual, and in vivo screening for an anti-tumor agent by imaging the tumor neovasculature in the individual (claimed). (I) is also useful for imaging normal and abnormal tissue and organs



including sites of primary and metastatic tumors and tumor neovasculature.

**ADMINISTRATION** - The **pharmaceutical compositions** can be administered systemically (e.g. intravenously), regionally, or locally (e.g. intra- or peri-tumorally or by intracystic injection), intraarterially, intratumorally, intravenously, parenterally, intra-pleurally, topically, orally or locally e.g. subcutaneously, intrathecally, or transmucosally (e.g. buccally, vaginally, rectally, nasally or mucosally), intra-tumorally (e.g. transdermally or locally). No dosage details given

**ADVANTAGE** - The chimeric molecule is capable of specifically binding to a lumen-expressed vascular endothelial cell protein. The chimeric molecule as an imaging enhancing agent, which enhances a computer assisted tomography (CAT) image, a magnetic resonance spectroscopy (MRS) image, a magnetic resonance imaging (MRI) image, a positron emission tomography (PET) image, a single-photon emission computed tomography (SPECT) image or a bioluminescence image (BLI) for a composition.

**EXAMPLE** - A chimeric recombinant polypeptide, an **RGD**-containing-luciferase fusion protein was produced in a bacterial expression system. The **RGD**-luciferase protein and, as a negative control, the reverse sequenced DGR fusion protein (DGR luciferase) were expressed. The **RGD**-luciferase protein had a strong tendency to multimerize (cyclize) due to reactive SH-groups on the terminal end of the peptide. This required production of the protein under dilute conditions. The recombinant proteins were purified and added to MDA-435 human breast carcinoma cells as given in Rahman (1989) J. Natl. Cancer Inst. 81:1794-1800 in culture wells. The MDA-435 cells, which expressed the **RGD** receptor on their cell surface, were useful for in vitro testing of this targeting approach for bioluminescent imaging (BLI). The chimeric **RGD**-luciferase protein were attached to the surface of the cells and could be detected using BLI. DGR-luciferase binding, serving as a control for possible nonspecific binding, could not be detected. The **RDG**-luciferase was also injected into a nude mouse with an orthotopic mammary tumor. Luciferin was administered. The animal was imaged in an in vivo bioluminescent imaging system. It was found that the presence of the tumor was detected by the emission of luciferase-produced photons from the tumor site. (35 pages)

L107 ANSWER 6 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-07859 BIOTECHDS

**TITLE:** Novel vector comprising double stranded DNA having target sequence and chimeric molecule comprising sequence specific polyamide moiety bound non-covalently to target and ligand moiety covalently linked to polyamide;  
vector-mediated gene transfer for expression in CHO cell culture, antisense, ribozyme and antibody for use in recombinant vaccine and nucleic acid vaccine preparation and gene therapy

**AUTHOR:** PESSI A; FATTORI D; INGALLINELLA P; BIANCHI E; KINZEL O

**PATENT ASSIGNEE:** IST RICERCHE BIOL MOLECOLARE ANGELETTI

**PATENT INFO:** WO 2001088160 22 Nov 2001

**APPLICATION INFO:** WO 2000-IB980 17 May 2000

**PRIORITY INFO:** GB 2000-11938 17 May 2000

**DOCUMENT TYPE:** Patent

**LANGUAGE:** English

**OTHER SOURCE:** WPI: 2002-106127 [14]

**AN** 2002-07859 BIOTECHDS

**AB** DERWENT ABSTRACT:

**NOVELTY** - A vector (conjugate) (I) comprising a double-stranded DNA (dsDNA) (Ia) having at least one target sequence (T); and a chimeric molecule (Ib) which comprises (i) a sequence specific polyamide (SSP) moiety bound non-covalently to (T); and (ii) a ligand moiety (L) covalently linked to SSP, is new.

**DETAILED DESCRIPTION** - **INDEPENDENT CLAIMS** are also included for the following: (1) a composition comprising (I) and a carrier; (2) synthesis (M1) of SSP on a solid support involving: (a) attaching an N-terminal of

the polyamide to the solid support via a safety-catch linker, -S(=O)<sub>2</sub>-NH-; and (b) following synthesis of the polyamide, removing it from the solid support by cleavage of the safety-catch linker by activation and nucleophilic attachment; (3) introducing (M2) a dsDNA into a cell or a sub-cellular compartment involving: (a) providing (Ib) which comprises SSP and (L) linked covalently to the SSP moiety, and capable of being directed to the cell or the sub-cellular compartment; (b) providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA to provide a vector; and (c) bringing the vector into contact with the cell under conditions for uptake of the vector and transport of the dsDNA; (4) a eukaryotic cell obtained by (M2); and (5) progeny of a eukaryotic cell obtained by (M2).

WIDER DISCLOSURE - Also disclosed are: (1) a chimeric molecule (chimera) which comprises SSP moiety capable of binding non-covalently to a target nucleic acid sequence and a ligand moiety linked covalently to the SSP moiety; and (2) compositions comprising (I) or (Ib).

BIOTECHNOLOGY - Preparation: (I) Is synthesized by the process which includes the step of synthesis of SSP by (M1). Preferred Vector: (I) Further comprises one or more sequences designed to facilitate homologous recombination to a specific locus within a host cell. (I) Comprises two or more (Ib) which comprise different ligand moieties. (Ia) has more than one (T) (in the range of 2-100, and preferably 6-10 target sequences), which is not present in the promoter or coding sequence part of the vector. (T) is at least 6 bases in length, preferably 10-20 bases in length. (Ia) Is linear, circular or a circular supercoiled DNA. (Ia) Further comprises dsDNA sequences of human, non-human animal, vegetable, bacterial or viral origin, and also comprises one or more transcribable sequences from promoters, and origins of replication, one or more selectable or detectable markers. (Ia) Comprises a transcribable DNA sequence which, when transcribed from the DNA under the control of a promoter (a) brings about an therapeutic effect, (b) yields mRNA for the expression of a protein, or (c) yields RNA which itself has a function as an anti-sense RNA or a ribozyme. (Ia) Comprises one or more coding sequences designed to modify tumor cells so that the tumor cells may be destroyed or inactivated. (Ia) Further comprises (a) one or more genes encoding enzymes capable of activating pro-drugs into active toxic drugs, (b) one or more tumor suppressor genes, (c) genes encoding cytokines or cell surface markers of immunoglobulin superfamily, (d) one or more functional copies of a gene, (e) DNA antigens useful as vaccines, or (f) one or more consecutive promoters and tissue specific promoters. SSP comprises at least 6 organic heterocyclic groups at least some of which are pyrrole and imidazole groups, preferably at least 7 organic heterocyclic groups (e.g. optionally substituted pyrrole, imidazole, pyrazole, triazole, furan, thiophene, oxazole, thiazole, or cyclopentadiene) or comprises 8-30 (preferably 18) organic cyclic groups. At least 60% (preferably 100%) of the organic cyclic groups or the organic heterocyclic groups which have 5 or 6 (preferably 5) annular members. The organic heterocyclic groups have 1-3 annular heteroatoms such as nitrogen, oxygen or sulfur. The organic heterocyclic groups have 1-2 annular nitrogen heteroatoms, and are preferably optionally substituted pyridine, pyrimidine, or triazine, where one or more annular NH groups are substituted with 1-3C alkyl groups (preferably Me). SSP comprises the organic heterocyclic groups (N-methyl pyrrole (Py) or N-methyl imidazole) having 5 annular members, and 1-2 annular nitrogen atoms of which one is methylated. The SSP further comprises one or more (2-6, preferably 4) optionally substituted aliphatic amino acid groups (e.g. glycine, beta alanine or gamma amino butyric acid) having a chain of 2-6 carbon atoms. The SSP comprises the optionally substituted amino acid group having a chain of 2-6 carbon atoms, proximal to one terminus of the moiety. (I) Comprises no consecutive sequence of 6 heterocycles, and where the organic cyclic groups and aliphatic amino acid groups, if present, are joined by linking groups having a length of 2 atoms where at least some of the linking groups will have NH groups. The linking groups are preferably methyleneamino (-CH<sub>2</sub>-NH-), carboxamide (-C(=O)NH-), ethylene (-CH<sub>2</sub>CH<sub>2</sub>-), thiocarboxamide (-C(=S)NH-), or carboxamidinoyl (-C(=NH)NH-). Preferably, the linking groups are carboxamide (preferred),

thiocarboxamide, or carboxamidinoyl. One or both of termini of SSP has a polar group (e.g. amino, hydroxyl, or mercapto) substituted on an alkyl group, where the polar group is from 2-6 carbon atoms from the linkage to the remaining molecule. At pH less than 8, the amino group is positively charged. Alternately, the polar group may also be optionally substituted aminopropyl or N-methylaminopropyl, where the SSP has one or two complementary pairs, each of which includes a N-methyl imidazole group and specificity of one nucleotide. (L) is capable of directing the conjugate to a cellular or subcellular location, preferably to the nucleus of a eukaryotic cell, in which case the ligand moiety is a general nuclear localization signal. (L) (a) is a protein or polypeptide capable of binding a target receptor, (b) is a protein or polypeptide based on hormones or other signaling proteins which bind to a target on the surface of a cell, or (c) comprises a hybrid protein which includes a component to direct the conjugate to a particular target cell, and a component to promote uptake of the conjugate by the cell. (L) is insulin, asialoglycoprotein or its synthetic analogues, transferrin, malaria circumsporozoite protein, **RGD** analogues or endoosmolytic peptide. The ligand moiety is a growth factor which binds to a receptor, or is an antibody or its fragment. (L) is a carbohydrate or mannose. Preferred Method: In (M1), the safety catch linker comprises a linkage  $-C(=O)-CH_2CH_2CH_2-S(=O)_2-NH-$ ,  $-C(=O)-CH_2CH_2CH_2-S(=O)_2-NH-C(=O)-$ . The activation is achieved by reaction with iodoacetonitrile. The nucleophilic attack is achieved by reaction with amine or thiol. The polyamide is synthesized using one or more of the reagents (R1), (R2) or (R3) as given in the specification.

ACTIVITY - Antibacterial; Virucide.

MECHANISM OF ACTION - Gene therapy; Vaccine. No biological data given.

USE - (I) Is useful in a method of treatment of the human or animal body and for preparing a medicament for treating a condition treatable by gene therapy. (I) Is also useful in gene therapy techniques. (M2) is useful for introducing a dsDNA into the nucleus of a eukaryotic cell which involves providing (Ib) which comprises SSP and (L) linked covalently to SSP moiety and capable of being directed to the nucleus of the eukaryotic cell; providing a dsDNA which includes a target sequence for the SSP moiety, under conditions where (Ib) binds to the dsDNA provide a vector; and bringing the vector into contact with the eukaryotic cell under conditions for uptake of the vector and transport of the dsDNA. The vector is brought into contact with the eukaryotic cell in vivo, ex vivo or in vitro. The eukaryotic cell is preferably a CHO cell (all claimed). (I) is also used to deliver DNA encoding antigens (viral antigens, bacterial antigens or host protein antigens) useful as vaccines.

ADMINISTRATION - **Pharmaceutical compositions** comprising (I) are administered by oral, rectal, nasal, topical, vaginal, or parenteral route. No dosage given.

EXAMPLE - Preparation of a sequence specific polyamide on a solid support using a safety catch linker was carried out by the following steps. Loading beta-Ala onto a resin via a safety catch linker, synthesis of a polyamide on the loaded resin, synthesis of a cleavage reagent, and cleavage of polyamide by the cleavage reagent. Loading of the first residue (beta-Ala) onto 4-sulfonamidobutyryl resin was carried out as follows. 9-fluorenylmethyloxycarbonyl (Fmoc)-beta-Ala-OH and diisopropylcarbodiimide (DIPC) (0.42 ml) were dissolved in 10 ml dichloromethane (DCM) and stirred. The solution was then filtered and added to 1.0 g of 4-sulfonamidobutyryl resin previously swollen in DCM, together with 330 mg of N',N'-dimethylamino-pyridine (DMAP). The mixture was stirred for 1 hour and then sequentially washed with DCM, N',N'-dimethylformamide (DMF), DCM. The procedure was **repeated** to obtain, after drying in vacuo for 2 hours, 1.37 g of resin. Solid-phase synthesis of polyamides was carried out as follows. The resin was pre-washed with 2 ml 20% piperidine in DMF and then followed by washes with DMF, DCM, 10% trifluoroacetic acid (TFA) in DCM and DCM, until the solution did not test acidic. Tert-butoxycarbonyl (BOC) cleavage was carried out using 1 ml of the cleavage mixture (80% TFA in

DCM, 0.5 M thiophenol). The resin was then washed with DCM and DMF. The resin from BOC cleavage was treated with 400 microliters of DIPEA, drained and immediately used for the next coupling. BOC-imidazole units were then coupled by the following process. 96 mg of 4-((tert-butoxycarbonyl)amino)-1-methylimidazole-2-carboxylic acid (0.4 mmol) and 55 mg of 1-hydroxy-7-azabenzotriazole (HOAt) were dissolved in 4 ml together with 77 mg (0.4 mmol) of water-soluble carbodiimide (WSCD) and 5 mg (0.04 mmol) of DMAP. The resulting solution was shaken for 10 minutes, and then added to the resin pre-swollen in DMF. Shaking was continued for 1 hour and then the resin was washed with 50 ml DMF and 50 ml DCM. Similarly coupling of HOAt activated BOC-pyrrole units and coupling of BOC-pyrrole-imidazole units were carried out. Coupling of BOC-beta-Ala-OH was done by dissolving 76 mg of BOC-beta-Ala-OH and 55 mg of HOAt in 4 ml DMF together with 77 mg (0.4 mmol) of WSCD and 5 mg (0.04 mmol) of DMAP. The resulting solution was added to the resin pre-swollen in DMF. The mixture was shaken for 1 hour and then washed with 50 ml DMF and 50 ml DCM. 2-(triphenylmethylthio)ethanoic acid (I) and mono 2-(triphenylmethylthio)ethanoyl derivative of 3,3'-diamino-N-methyldipropylamine (II) were prepared for cleavage from the safety-catch linker. Cleavage of the polyamide (III) from the resin was carried out as follows. A batch of resin containing the sequence (resin)beta-Ala-Pyr-Im-beta-Ala-Pyr-Im-gamma amino butyric acid-Pyr-Im-beta-Ala-Pyr-Im, (Im = N-methyl imidazole, Pyr = pyrrole) synthesized according to the above procedure was treated with 0.72 ml iodoacetonitrile and 0.42 ml diisopropylethylamine (DIEA) in 2 ml N-methylpyrrolidone (NMP) for 4 hours, then washed with NMP, DCM and dried. A solution of (II) and DIEA in 0.4 ml DMF was then added and the resin was stirred. The solution was filtered and concentrated. The oily residue was dissolved in 5 ml DMF and treated with 200 mg PS-isocyanate resin for 2 hours. Filtration and concentration in vacuo afforded a yellow oil. The residue was dissolved in 10 ml of a TFA/DCM (1:1 v/v) solution containing 10% triisopropylsilane (TIPS). Concentration in vacuo yielded an oily residue, which was triturated with diethylether to obtain 95 mg of a yellow oil which were then purified by size-exclusion chromatography. The rhodamine labeled bromoacetyl-nuclear localization signal (NLS) peptide (IV) and (III) (0.72 mg) were dissolved in 200 microliters of DMF and 2 microliters DIEA. The reaction was monitored by analytical high performance liquid chromatography (HPLC). After 30 minutes the reaction was complete and the solution was immediately purified by HPLC. The ability of peptide-polyamide conjugates to bind the DNA was assessed by circular dichroism (CD) spectroscopy and by gel electrophoresis and results showed that interactions between the polyamide and the DNA. (98 pages)

L107 ANSWER 7 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-06674 BIOTECHDS

TITLE: Complex for transfecting cell with nucleic acid for treating, preventing conditions caused by deficiency in a gene in humans, has nucleic acid, lipid, integrin binding and polycationic nucleic acid-binding components; hematopoietic stem cell transfection with green fluorescent protein enables gene therapy, nucleic acid vaccine application and antisense therapy

AUTHOR: HART S L

PATENT ASSIGNEE: ICH PRODN LTD

PATENT INFO: WO 2001092542 6 Dec 2001

APPLICATION INFO: WO 2000-GB2394 30 May 2000

PRIORITY INFO: US 2001-287410 1 May 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-139612 [18]

AN 2002-06674 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - A complex (I) comprising a nucleic acid, an integrin binding component, a polycationic nucleic acid-binding component and a lipid component, is new. The integrin binding component comprises an

integrin-binding element and a spacer element.

**DETAILED DESCRIPTION** - A complex (I) comprising a nucleic acid, an integrin binding component, a polycationic nucleic acid-binding component and a lipid component, is new. The integrin binding component comprises an integrin-binding element and a spacer element longer and/or more hydrophobic than the dipeptide spacers GG (glycine-glycine) and GA (glycine-alanine). **INDEPENDENT CLAIMS** are also included for the following: (1) an integrin binding peptide (II); (2) a mixture (III) comprising an integrin binding component, and a polycationic nucleic acid-binding component; (3) producing (I), by admixing the components or incorporating a nucleic acid with (III); (4) a complex obtained by the method of (3); (5) a **pharmaceutical composition** comprising (I); (6) a kit comprising an integrin binding component, a polycationic nucleic acid-binding component, and optionally an agent that disrupts cell-cell functions; and (7) a spacer peptide (S1). (S1) is XSXGA. S = serine; A = alanine; G = glycine; and X = epsilon-amino hexanoic acid.

**WIDER DISCLOSURE** - A cell transfected with (I) and progeny of the cell are disclosed as new.

**BIOTECHNOLOGY** - Preferred Complex: The spacer element of the integrin-binding component is a peptide, preferably a dipeptide or comprises more than 2 naturally occurring or synthetic amino acids. The spacer element is at the N-terminus of the integrin-binding element. The integrin-binding element is an integrin-binding peptide containing or comprising all or part of the integrin-binding domain of a naturally-occurring integrin ligand. The peptide comprises the conserved amino acid sequence arginine-glycine-aspartic acid (**RGD**), and has two or more cysteine residues that form one or more disulfide bonds, forming a cyclic peptide. The peptide is an **RGD** containing peptide having a cyclic region in which the conformational freedom of the **RGD** sequence is restricted. The nucleic acid component is or relates to a gene that is the target for gene therapy, gene vaccination or anti-sense therapy and comprises all or part of the coding sequence of the gene. The nucleic acid also comprises transcriptional and/or translational control elements, and is optionally packed in a phage or vector. The nucleic acid binding component has 3-100 cationic monomers and the polycationic component is an oligolysine having 10-20, preferably 16, 17 or 18 lysine residues. The lipid component is or is capable of forming a cationic liposome and comprises one or more lipids chosen from cationic lipids and lipids having membrane destabilizing or fusogenic properties. The lipid is or comprises the neutral lipid dioleyl phosphatidyl-ethanolamine (DOPE), the cationic lipid N-(1-(2,3-diolexyloxy)propyl)-N,N,N-trimethylammonium chloride (DOTMA) or 2,3-diolexyloxy-N-(2-(spermidinecarboxamido) ethyl)-N,N-dimethyl-1-propanaminium-trifluoroacetate (DOSPA) or a lipid having similar properties. The lipid component is a mixture of DOPE and DOTMA, especially their equimolar mixture or DOPE and DOSPA in the ratio of 1:3. (I) comprises an equimolar mixture of DOPE and DOTMA/DOSPA as lipid component, integrin-binding peptide as integrin-binding component and (K)16 as the polycationic nucleic acid-binding component, where the ratio of lipid component:integrin-binding/polycationic nucleic acid-binding component:nucleic acid is 0.75 (DOPE and DOTMA):4:1 by weight or 0.5:1.25:0.25 nmol on a molar basis or 12 (DOPE and DOSPA):4:1 by weight.

**ACTIVITY** - Antiasthmatic; Virucide; Anti-HIV (human immunodeficiency virus); Cytostatic; Ophthalmological; Vasotropic.

**MECHANISM OF ACTION** - Gene therapy; Antisense therapy; Vaccine. Tissue culture of rat primary smooth muscle cells and cardiac myocytes were prepared. A lipofectin-peptide-DNA (LID) complex comprising lipofectin, (K)16-peptide (GlyAlaCysArgArgGluThrAlaTrpAlaCysGly) and green fluorescent protein (GFP) as a reporter gene in the optimal LID ratio was prepared. The tissue cultures were transfected with the complex. Fluorescence imaging of GFP-expressing cells demonstrated transfection efficiency in excess of 50 %. Primary smooth muscle cells and cardiac myocytes were particularly resistant to plasmid-mediated transfection using other non-viral vectors. In contrast, the transfection complex achieved transfection efficiencies in excess of 50 %, thus

demonstrating the use of the complexes for treatment of diseases affecting muscle, including smooth muscle and cardiac muscle.

USE - (I) is useful for transfecting cells in vitro or in vivo with a nucleic acid, for treatment or prophylaxis of a condition caused in human or a non-human animal by a defect and/or a deficiency in a gene, immunization and antisense therapy of a human or a non-human animal. The cells are confluent, slowly dividing or non-dividing cells, a confluent monolayer or a tissue comprising such cells, preferably an endothelium or an epithelium. The cells are also contacted with an agent capable of disrupting cell-cell junctions like calcium-binding or calcium chelating agent, preferably EGTA (ethylene glycol-bis (beta-aminoethyl ether)-N,N,N',N'-tetraacetic acid) or an antibody to a substance involved in cell adhesion, preferably anti-cadherin. EGTA is used at a concentration of 1 mM or less, preferably 0.5-1, more preferably 1 mM in vitro or 25-200 nM, preferably 100 nM, in vivo. The agent is used in conjunction with the complex. (All claimed). (I) is useful for transfecting bronchial and lung epithelium and corneal endothelium for gene therapy for cystic fibrosis, asthma and also various cancers and viral infections for example human immunodeficiency virus (HIV) infection. (I) is useful as a vaccine or for therapy of neuroblastoma and the effective transfection of primary smooth muscle cells, cardiac myocytes and hematopoietic cells demonstrate that diseases and other pathological conditions affecting such cells can be treated by gene therapy. Hematopoietic cell transfection enables gene therapy, gene vaccination and anti-sense therapy of diseases involving hematopoietic cells, including leukemia and bone marrow stem cell disorders, for example transfection of a cytokine gene may be used for adjuvant immunotherapy. Transfection of corneal endothelium is useful for treatment of eye disease affecting the cornea or corneal organ transplants, for example in glaucoma. A gene that prevents proliferation of cells in blood vessel walls is introduced using (I) to reduce restenosis.

ADVANTAGE - (I) enhances the transfection efficiency and hence the effectiveness of the treatment of epithelial and endothelial tissues, and is effective in transporting large DNA molecules, for example DNA larger than 125 kbase, which is particularly difficult using conventional vectors and enables introduction of artificial chromosomes into cells.

EXAMPLE - Transfection complexes were prepared by mixing solutions of oligolysine-peptide ((K)16 GlyAlaCysArgGlyAspMetPheGlyCysAla) at 0.1 mg/ml in OptiMEM low serum tissue culture medium with a solution of lipofectin (N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethyl ammonium chloride (DOTMA)/dioleoyl phosphatidyl-ethanolamine (DOPE) cationic liposome) in a range of concentrations from 1-10 micro-g/100 micro-l in OptiMEM. pGL2 (containing luciferase reporter gene)-control plasmid DNA (0.1 mg/ml) was added and mixed by **repeated** pipetting. The ratio of mixing of each component was a constant 4 micro-g of oligolysine-peptide per micro-g of DNA, while the proportion of lipofectin varied from 1-10 micro-g/micro-g of DNA. ECV304 cells were transfected with the complexes, incubated for 48 hours and assayed for luciferase expression. The results showed that complexes formed with 1 micro-g of lipofectin and 4 micro-g of oligolysine-peptide/micro-g of plasmid were 100-fold more active than complexes lacking lipofectin. Addition of larger amounts of lipofectin reduced transfection activity in a lipofectin dose-dependent manner. (108 pages)

L107 ANSWER 8 OF 18 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN

ACCESSION NUMBER: 2002-05354 BIOTECHDS

TITLE: Transfecting confluent cells with nucleic acid for gene therapy or gene vaccination, comprises contacting the cells with a receptor-targeted vector having the nucleic acid and an agent that disrupts cell-cell junctions;  
vector expression in host cell useful in cell transfer gene therapy

AUTHOR: HART S L

PATENT ASSIGNEE: ICH PRODN LTD

PATENT INFO: WO 2001092543 6 Dec 2001

APPLICATION INFO: WO 2000-GB2396 30 May 2000

PRIORITY INFO: US 2001-287410 1 May 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-114355 [15]

AN 2002-05354 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Transfecting (I) confluent cells or other slowly dividing or non-dividing cells that are in contact with each other, with a nucleic acid, comprises contacting the cells with a receptor-targeted vector (RTV) comprising the nucleic acid, and an agent (A) that disrupts cell-cell junctions under conditions suitable to effect transfection.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an integrin targeting transfection vector complex (II) comprising an integrin binding peptide which consists of or comprises any one of the sequences (S1) - (S12); (2) confluent cells (III) or other slowly dividing or non-dividing cells that are in contact with each other, transfected with a nucleic acid, and also the progeny of such cells; (3) a disease model (IV) for use in testing candidate pharmaceutical agents, comprising (III); (4) a **pharmaceutical composition** (V) which may be a vaccine comprising RTV and (A), in admixture or conjunction with a pharmaceutically suitable carrier; (5) use of RTV and (A) for the manufacture of a medicament for the prophylaxis of a condition caused in a human or in a non-human animal by a defect and/or a deficiency in a gene, for therapeutic or prophylactic immunization of a human or of a non-human animal, or for antisense therapy of a human or of a non-human animal; (6) a kit comprising RTV and (A); and (7) a kit comprising (A) and an integrin-binding component, a polycationic nucleic acid-binding component and a lipid component and further comprising either a nucleic acid or a plasmid or vector suitable for expression of a nucleic acid, the plasmid or vector being empty or comprising the nucleic acid. Cys Arg Gly Asp Met Phe Gly Cys (S1) Cys Arg Gly Asp Met Phe Gly Cys Gly (S2) Cys Arg Gly Asp Met Phe Gly Cys Ala (S3) Cys Asp Cys Arg Gly Asp Cys Phe Cys Ala (S4) Cys Arg Arg Glu Thr Ala Trp Ala Cys Ala (S5) Cys Arg Arg Glu Thr Ala Trp Ala Cys (S6) Cys Arg Arg Glu Thr Thr Ala Trp Ala Cys (S7) Cys Arg Arg Glu Thr Ala Trp Ala Cys Gly (S8) Cys Arg Gly Asp Met Phe Gly Cys Gly Gly (S9) Gly Pro Glu Ile Leu Asp Val Pro Ser Thr (S10) Cys Gln Ile Asp Ser Pro Cys Ala (S11) Cys Arg Arg Glu Thr Ala Trp Ala Cys Gly Lys Gly Ala Cys Arg Arg Glu Thr Ala Trp Ala Cys Gly (S12)

BIOTECHNOLOGY - Preferred Agent: (A) capable of disrupting cell-cell junctions is a calcium-binding or calcium chelating agent, preferably EGTA (ethylene glycol-bis (beta-aminoethyl ether)-N,N,N',N'-tetraacetic acid) used at a concentration of 1 mM or less, for e.g., 0.5 - 1 mM, especially 1 mM in vitro or 25 - 200 mM, for e.g. 100 mM, in vivo, or an antibody directed to a substance involved in cell adhesion, preferably an anti-cadherin. (A) is used at the same or at substantially the same time as the vector. Preferred Vector: RTV is a non-viral vector that is targeted to a cell-surface receptor, preferably insulin, asialoglycoprotein or transferrin receptor, or to a receptor on neuroblastoma cells, is folate conjugated to liposomes or is galactose for targeting liver cells. RTV is targeted against an integrin receptor and is an integrin targeting transfection vector complex comprising: (a) nucleic acid; (b) an integrin-binding component, especially an integrin-targeting peptide comprising the conserved amino acid sequence arginine-glycine-aspartic acid (RGD); (c) a polycationic nucleic acid-binding component, especially an oligolysine having 10-20, especially 16, 17 or 18 lysine residues; and (d) a lipid component, especially DOPE (dioleoyl phosphatidylethanolamine), DOTMA (N-(1-(2,3-dioleoyloxy)propyl)-N,N,N-trimethylammonium chloride), DOSPA (2,3-dioleoyloxy-N-(2-(spermidinecarboxamido) ethyl)-N,N-dimethyl-1-propanaminiumtrifluoroacetate) or their combinations. The integrin-binding peptide has at least two cysteine residues that form one or more double bond(s), forming a cyclic peptide and comprises a spacer element that is glycine-glycine (GG), glycine-alanine (GA) or is longer and/or more hydrophobic than the spacers GG and GA. The spacer element is

XSXGA, in which X is epsilon-amino hexanoic acid.

ACTIVITY - Antiasthmatic; virucide; anti-HIV; cytostatic; ophthalmological; vasotropic.

MECHANISM OF ACTION - Vaccine; gene therapy. Lipid (lipofectin) (1 mg/ml) and peptide (Gly Ala Cys Arg Arg Glu Thr Ala Trp Ala Cys Gly) (1 mg/ml) were mixed in one tube, and pCILuc plasmid DNA (1 mg/ml) and EGTA in phosphate buffered saline (PBS) were mixed together in another tube. Then the contents of the two tubes were mixed so that the final ratios were 0.75 micrograms lipid to 1 microg DNA and a final concentration of 100 mM EGTA (or no EGTA for the control). The protocol was repeated to give vector complexes having a final EGTA concentration of 400 mM. Each mouse received 8 microg of plasmid DNA in a volume of 50 microliters. The vector/EGTA mixture was administered to the mouse lung by intratracheal instillation. 1, 3 and 7 days following the intratracheal instillation, the mice were killed by cervical dislocation and the lungs perfused by the inferior venacava with heparinized PBS until free of blood. Cell lysis buffer was added to each lung (4 microliters/mg). The tissue was then homogenized. Lung homogenates were centrifuged, 20 microliters of the supernatant were added to 100 microliters of luciferase assay buffer and luminescence was measured. The total protein concentration in the lysate was measured. Luciferase activity was expressed in relative light units (RLU) for each sample of lung lysate minus the background and normalized per mg of protein. The results showed that in the presence of 100 mM EGTA, transfection was enhanced four-fold. But 400 mM proved lethal in many cases.

USE - (I) is useful for transfecting confluent cells or other slowly dividing or non-dividing cells that are in contact with each other, especially epithelial or endothelial cells, with a nucleic acid, for expressing the nucleic acids and for protein production in the host cells. A pharmaceutical composition (V) is useful for treatment or prophylaxis of a condition caused in a human or in a non-human animal by a defect and/or a deficiency in a gene (claimed). (I) is useful for transfecting bronchial and lung epithelium and corneal endothelium for gene therapy for cystic fibrosis, asthma and also various cancers and viral infections for e.g. human immunodeficiency virus (HIV) infection. Neuroblastoma cells, primary smooth muscle cells, cardiac myocytes and hematopoietic cells are transfected with high efficiency, and diseases and other pathological conditions affecting them are treated. Hematopoietic cell transfection enables gene therapy, gene vaccination and anti-sense therapy of diseases involving hematopoietic cells, including leukemia and bone marrow stem cell disorders, for e.g. transfection of a cytokine gene may be used for adjuvant immunotherapy. Transfection of corneal endothelium is useful for treatment of eye disease affecting the cornea or corneal organ transplants, for e.g. in glaucoma. A gene that prevents proliferation of cells in blood vessel walls is introduced using an integrin targeting transfection vector complex (II) to reduce restenosis. (II) is useful for intracellular transport and delivery of anti-sense oligonucleotides, which enables antiviral and cancer therapy. Confluent cells (III) are useful in drug testing.

ADMINISTRATION - No administration details are given.

ADVANTAGE - (I) enhances the transfection efficiency and hence the effectiveness of the treatment of epithelial and endothelial tissues. An integrin targeting transfection vector complex (II) is effective in transporting large DNA molecules, for e.g. DNA larger than 125 kb, which is particularly difficult using conventional vectors and enables introduction of artificial chromosomes into cells. (111 pages)

L107 ANSWER 9 OF 18 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: AAU96866 peptide DGENE

TITLE: Enhancing angiogenesis to treat diseases associated with deficient angiogenesis, such as wound healing disorders, comprises administering an integrin binding pro-angiogenic agent, e.g., neural cell adhesion molecule L1 -

INVENTOR: Montgomery A; Brooks P; Reisfeld R A

PATENT ASSIGNEE: (SCRI)SCRIPPS RES INST.



PATENT INFO: WO 2002028355 A2 20020411 42p  
APPLICATION INFO: WO 2001-US42375 20010926  
PRIORITY INFO: US 2000-237739P 20001002  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: 2002-416623 [44]  
DESCRIPTION: Mutated human neural cell adhesion molecule L1 RGD motif.

AN AAU96866 peptide DGENE

AB The invention relates to a method of enhancing angiogenesis (M1), comprises administering an integrin binding pro-angiogenic agent to a mammal, where angiogenesis is desirable, to enhance angiogenesis in the mammal. Also included are an isolated protein or peptide consisting of the entire extracellular domain of the NCAM L1 (neural cell adhesion molecule) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a NCAM L1 comprising the Ig-like domains 4-6 (Ig 4-6) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a protein or a peptide that specifically binds to an antibody that is raised against the present sequence, a **pharmaceutical composition** comprising an isolated protein or peptide and a pharmaceutically acceptable carrier or excipient and an isolated nucleic acid encoding the protein or peptide of. M1 is used to enhance angiogenesis in a mammal, such as a human to treat disorders or diseases associated with deficient angiogenesis, such as ischaemic diseases or wound healing disorders, by administering an integrin binding pro-angiogenic agent to the mammal. The present sequence is a mutant human neural cell adhesion molecule L1 **RGD** (Arg-Gly-Asp) **motif** peptide which has reduced proangiogenic function compared to the wild-type peptide.

L107 ANSWER 10 OF 18 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: AAU96865 peptide DGENE

TITLE: Enhancing angiogenesis to treat diseases associated with deficient angiogenesis, such as wound healing disorders, comprises administering an integrin binding pro-angiogenic agent, e.g., neural cell adhesion molecule L1 -

INVENTOR: Montgomery A; Brooks P; Reisfeld R A

PATENT ASSIGNEE: (SCRI)SCRIPPS RES INST.

PATENT INFO: WO 2002028355 A2 20020411 42p

APPLICATION INFO: WO 2001-US42375 20010926

PRIORITY INFO: US 2000-237739P 20001002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2002-416623 [44]

DESCRIPTION: Human neural cell adhesion molecule L1 RGD motif.

AN AAU96865 peptide DGENE

AB The invention relates to a method of enhancing angiogenesis (M1), comprises administering an integrin binding pro-angiogenic agent to a mammal, where angiogenesis is desirable, to enhance angiogenesis in the mammal. Also included are an isolated protein or peptide consisting of the entire extracellular domain of the NCAM L1 (neural cell adhesion molecule) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a NCAM L1 comprising the Ig-like domains 4-6 (Ig 4-6) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a protein or a peptide that specifically binds to an antibody that is raised against the present sequence, a **pharmaceutical composition** comprising an isolated protein or peptide and a pharmaceutically acceptable carrier or excipient and an isolated nucleic acid encoding the protein or peptide. M1 is used to enhance angiogenesis in a mammal, such as a human to treat disorders or diseases associated with deficient angiogenesis, such as ischaemic diseases or wound healing disorders, by administering an integrin binding pro-angiogenic agent to the mammal. The present sequence is a human neural cell adhesion molecule L1 **\*\*\*RGD\*\*\*** (Arg-Gly-Asp) **motif** which retains integrin binding function.

L107 ANSWER 11 OF 18 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: AAY67526 peptide DGENE

TITLE: Compositions containing antibody to filamentous hemagglutinin, used e.g. to increase permeability of the blood-brain barrier and to inhibit inflammation or bacterial adhesion -

INVENTOR: Masure H R; Tuomanen E

PATENT ASSIGNEE: (UYRQ)UNIV ROCKEFELLER.

PATENT INFO: US 6015560 A 20000118 82p

APPLICATION INFO: US 1995-465966 19950606

PRIORITY INFO: US 1994-348353 19941130

WO 1992-US3725 19920504

US 1991-695613 19910503

US 1994-247572 19940523

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-181133 [16]

DESCRIPTION: FHA peptide containing RGD motif.

AN AAY67526 peptide DGENE

AB The invention provides a novel **pharmaceutical composition** for increasing the permeability of the blood-brain barrier to a molecule (I). The composition comprises (I) and an antibody to FHA (filamentous hemagglutinin) which binds to endothelial cells in brain blood vessels, increasing permeability. FHA contains polypeptide regions with binding properties similar to those of complement C3bi, factor X and integrin receptor CR3, and some anti-FHA antibodies are competitive inhibitors of these materials, i.e. they reduce leukocyte migration or bacterial adhesion. The compositions are used to improve delivery of (I) to the brain, e.g. where (I) is used to treat brain cancer, acquired immune deficiency syndrome, epilepsy, Parkinson's or Alzheimer's diseases or other neurological diseases. Other antibodies directed against particular regions of FHA are used to treat inflammation (caused by microbial infection or auto-immune disease), also to prevent adhesion of Bordetella pertussis to respiratory endothelial cells. The present sequence represents a FHA peptide containing a **RGD motif**.

L107 ANSWER 12 OF 18 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: AAY79413 Protein DGENE

TITLE: Novel proteins and polynucleotides representing contortrostatin useful for inhibiting platelet aggregation, tumour metastasis and growth -

INVENTOR: Markland F S; Zhou Q

PATENT ASSIGNEE: (UYSC-N)UNIV SOUTHERN CALIFORNIA.

PATENT INFO: WO 2000018421 A1 20000406 81p

APPLICATION INFO: WO 1999-US22608 19990929

PRIORITY INFO: US 1998-163047 19980929

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-303389 [26]

CROSS REFERENCES: N-PSDB: AAZ94881

DESCRIPTION: Southern copperhead snake contortrostatin.

AN AAY79413 Protein DGENE

AB The present sequence is that of the Southern copperhead snake venom disintegrin, contortrostatin, a protein that inhibits the interactions between integrins and their receptors. The sequence was deduced from isolated snake venom cDNA (see AAZ94881). The contortrostatin precursor protein includes a pro-protein region, a metalloproteinase region which includes a metal-binding **motif**, and a disintegrin region which includes an **RGD** loop that acts as an integrin antagonist. Polypeptides comprising the pro-region, the metalloproteinase region, and the contortrostatin monomer, as well as the full-length precursor protein, can be obtained using recombinant DNA methods. The purified proteins are used in **pharmaceutical compositions** for treating diseases associated with an integrin binding to an integrin receptor,

especially to inhibit platelet aggregation, tumour metastasis, angiogenesis, neovascularization, cell adhesion, invasiveness, or growth (all claimed). The proteins are also useful for treating a thrombotic disorder, e.g. preventing arterial, venous, and microvascular thrombosis and thromboembolism, stroke, transient ischaemic attacks, arteriosclerosis, atherosclerosis, pulmonary embolism, aneurism, angina and myocardial infarction.

L107 ANSWER 13 OF 18 DGENE COPYRIGHT 2003 THOMSON DERWENT on STN

ACCESSION NUMBER: AAZ94881 cDNA DGENE

TITLE: Novel proteins and polynucleotides representing contortrostatin useful for inhibiting platelet aggregation, tumour metastasis and growth -

INVENTOR: Markland F S; Zhou Q

PATENT ASSIGNEE: (UYSC-N)UNIV SOUTHERN CALIFORNIA.

PATENT INFO: WO 2000018421 A1 20000406 81p

APPLICATION INFO: WO 1999-US22608 19990929

PRIORITY INFO: US 1998-163047 19980929

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-303389 [26]

CROSS REFERENCES: P-PSDB: AAY79413

DESCRIPTION: Southern copperhead snake contortrostatin cDNA.

AN AAZ94881 cDNA DGENE

AB The present sequence is that of claimed DNA encoding the Southern copperhead snake venom disintegrin, contortrostatin (see AAY79413), a protein that inhibits the interactions between integrins and their receptors. The DNA was obtained from a venom gland cDNA library by PCR amplification using primers (see AAZ94882-83) based on a conserved region of disintegrins. Contortrostatin precursor protein includes a pro-protein region, a metalloproteinase region which includes a metal-binding motif, and a disintegrin region which includes an RGD loop that acts as an integrin antagonist. DNA molecules consisting of nucleotides 1341-1535 (encoding the disintegrin), 657-1316 (metalloproteinase), 87-656 (pro-protein) and 87-1535 (entire precursor protein) of the present sequence are also claimed. These can be used in the recombinant production of contortrostatin proteins. The purified proteins are used in **pharmaceutical compositions** for treating diseases associated with an integrin binding to an integrin receptor, especially to inhibit platelet aggregation, tumour metastasis, angiogenesis, neovascularization, cell adhesion, invasiveness, or growth (all claimed). The proteins are also useful for treating a thrombotic disorder, e.g. preventing arterial, venous, and microvascular thrombosis and thromboembolism, stroke, transient ischaemic attacks, arteriosclerosis, atherosclerosis, pulmonary embolism, aneurism, angina and myocardial infarction.

L107 ANSWER 14 OF 18 USPATFULL on STN

ACCESSION NUMBER: 2002:227655 USPATFULL

TITLE: Compositions and methods for in situ and in vivo imaging of cells and tissues

INVENTOR(S): Chinnaiyan, Arul M., Canton, MI, UNITED STATES  
Rehemtulla, Alnawaz, Plymouth, MI, UNITED STATES  
Ross, Brian D., Ann Arbor, MI, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002122806	A1	20020905
APPLICATION INFO.:	US 2001-734628	A1	20010305 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	GREGORY P. EINHORN, FISH & RICHARDSON P.C., Suite 500, 4350 La Jolla Village Drive, San Diego, CA, 92122		
NUMBER OF CLAIMS:	60		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Page(s)		

LINE COUNT: 1313  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides compositions and methods for imaging cells and tissues in vivo and in situ. Compositions and methods are provided for administration to enhance the imaging of cells and tissues by, e.g., computer assisted tomography (CAT), magnetic resonance spectroscopy (MRS), magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), or bioluminescence imaging (BLI). Thus, the invention provides compositions and methods for identifying sites of primary and metastatic tumors and tumor neovasculature.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L107 ANSWER 15 OF 18 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 2003-221770 [21] WPIDS  
DOC. NO. NON-CPI: N2003-176839  
DOC. NO. CPI: C2003-056536  
TITLE: Inhibiting amyloid toxicity or the formation of an amyloid deposit, comprises administering an agent that binds to an integrin, integrin subunit, or laminin.  
DERWENT CLASS: B04 D16 Q74  
INVENTOR(S): PRENNER, I G; RYDEL, R; WRIGHT, S; YEDNOCK, T  
PATENT ASSIGNEE(S): (PREN-I) PRENNER I G; (RYDE-I) RYDEL R; (WRIG-I) WRIGHT S; (YEDN-I) YEDNOCK T; (ELAN-N) ELAN PHARM INC  
COUNTRY COUNT: 100  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003006893	A2	20030123	(200321)*	EN	43
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					

US 2003109435 A1 20030612 (200340)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003006893	A2	WO 2002-US19803	20020708
US 2003109435	A1 Provisional	US 2001-304315P	20010709
	Provisional	US 2001-341772P	20011217
		US 2002-190548	20020709

PRIORITY APPLN. INFO: US 2001-341772P 20011217; US 2001-304315P 20010709; US 2002-190548 20020709

AN 2003-221770 [21] WPIDS

AB WO2003006893 A UPAB: 20030328

NOVELTY - Inhibiting amyloid toxicity or the formation of an amyloid deposit, comprising administering a dosage of one or more agent(s) that bind(s) to a molecule selected from an integrin subunit such as alpha 2, alpha v, alpha 6 or beta 1, an integrin such as alpha 2 beta 1, alpha 6 beta 1 or alpha v beta 1, and laminin, under conditions such that the agent(s) inhibit amyloid toxicity or the formation of an amyloid deposit, is new.

ACTIVITY - Nootropic; Neuroprotective; Antidiabetic; Antiparkinsonian.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The method is useful for inhibiting amyloidogenic protein

toxicity, inhibiting the formation of an amyloidogenic protein deposit and/or treating amyloidogenic diseases, such as Alzheimer's disease, type II diabetes, Parkinson's disease, a disease caused all or in part by prion infection, hereditary or systemic amyloidosis, or Down's syndrome.  
Dwg.0/9

L107 ANSWER 16 OF 18 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 2002-643417 [69] WPIDS  
DOC. NO. CPI: C2002-181737  
TITLE: New product comprising a dendroaspin scaffold and a serine protease inhibitor domain ligated to the dendroaspin scaffold, useful for treating or preventing diseases associated with thrombosis, e.g. myocardial infarction, stroke.  
DERWENT CLASS: B04 D16  
INVENTOR(S): KAKKAR, V V; LU, X  
PATENT ASSIGNEE(S): (TRIG-N) TRIGEN LTD  
COUNTRY COUNT: 100  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002063017	A2	20020815	(200269)*	EN	68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002063017	A2	WO 2002-GB500	20020205

PRIORITY APPLN. INFO: US 2001-267234P 20010205

AN 2002-643417 [69] WPIDS

AB WO 200263017 A UPAB: 20021026

NOVELTY - A product comprising a dendroaspin scaffold and a second portion comprising a serine protease inhibitor domain ligated to the dendroaspin scaffold, is new. The dendroaspin scaffold optionally has the native RGD motif deleted or replaced. The amino acid sequence has no integrin-binding activity or an integrin-binding amino acid sequence, and comprises a tripeptide sequence other than RGD containing D or E adjacent to G.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a polyamino acid comprising a nematode anticoagulant protein (NAP)-based domain having serine protease inhibitor activity linked through a proline-containing domain to another domain having integrin binding activity;
- (2) a hybrid polyamino acid comprising two domains, not derived from the same native molecule, interlinked by a linker comprising an imino acid residue;
- (3) a nucleic acid molecule encoding the polypeptide product cited above;
- (4) a plasmid comprising the nucleic acid in (3);
- (5) plasmid pGEX-3X comprising the nucleic acid in (3);
- (6) a host cell transformed with the plasmid in (5);
- (7) a cell culture comprising the host cell in (6);
- (8) producing the novel polypeptide product, comprising culturing the host cell in (6) to express the polypeptide, extracting the polypeptide from the culture and purifying it;
- (9) producing a polypeptide comprising an integrin-binding protein,

or its homolog;

(10) a polypeptide product obtainable by the methods of (8) or (9);

(11) a pharmaceutical composition comprising any of the polypeptide products;

(12) treatment or prophylaxis of a disease associated with thrombosis in a human or animal patient, comprising administering to the patient an effective amount of the pharmacologically active product;

(13) a linker comprising an amino acid sequence selected from Aa1-Gly and Gly-Aa1, where Aa1 is an imino acid;

(14) a linker which comprises at least two non-adjacent imino acids; and

(15) a product comprising first and second biologically active moieties linked through the linker.

ACTIVITY - Thrombolytic; Cardiant; Cerebroprotective.

No biological data is given.

MECHANISM OF ACTION - Serine protease inhibitor; Factor Xa inhibitor.

USE - The product is useful for the manufacture of a medicament for the treatment or prophylaxis of diseases associated with thrombosis, e.g. thrombosis, myocardial infarction, retinal neovascularization, endothelial injury (claimed), stroke, pulmonary embolism.

ADVANTAGE - The invention provides compounds that are orally active and have rapid onset of activity and low toxicity as compared to various agents for preventing blood clots, e.g. aspirin, dipyridamole and filopidine, which have a potential side effect of causing prolonged bleeding.

Dwg.0/3

L107 ANSWER 17 OF 18 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 2002-416623 [44] WPIDS  
DOC. NO. CPI: C2002-117517  
TITLE: Enhancing angiogenesis to treat diseases associated with deficient angiogenesis, such as wound healing disorders, comprises administering an integrin binding pro-angiogenic agent, e.g., neural cell adhesion molecule L1.  
DERWENT CLASS: B04 D16  
INVENTOR(S): BROOKS, P; MONTGOMERY, A; REISFELD, R A  
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST  
COUNTRY COUNT: 97  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2002028355	A2	20020411	(200244)*	EN	42
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ					
NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK					
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR					
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO					
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002011824	A	20020415	(200254)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
-----			
WO 2002028355	A2	WO 2001-US42375	20010926
AU 2002011824	A	AU 2002-11824	20010926

FILING DETAILS:

PATENT NO	KIND	PATENT NO
-----		
AU 2002011824	A Based on	WO 2002028355

PRIORITY APPLN. INFO: US 2000-237739P 20001002

AN 2002-416623 [44] WPIDS  
AB WO 200228355 A UPAB: 20020711  
NOVELTY - Enhancing angiogenesis (M1), comprises administering an integrin binding pro-angiogenic agent to a mammal, where angiogenesis is desirable, to enhance angiogenesis in the mammal, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated protein or peptide consisting of the entire extracellular domain of the NCAM L1 or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a NCAM L1 comprising the Ig-like domains 4-6 (Ig 4-6) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a protein or a peptide that specifically binds to an antibody that is raised against a peptide or a peptide having the fully defined amino sequence S1 given in specification;

(2) a pharmaceutical composition (I) comprising an isolated protein or peptide and a pharmaceutically acceptable carrier or excipient;

(3) an isolated nucleic acid encoding a protein or peptide consisting of the entire extracellular domain of the NCAM L1 or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a NCAM L1 comprising the Ig-like domains 4-6 (Ig 4-6) or a functional derivative or fragment that substantially retains its binding affinity with the integrin, a protein or a peptide that specifically binds to an antibody that is raised against a peptide having the amino sequences S1 or S2;

(4) a pharmaceutical composition (II) comprising a nucleic acid and a pharmaceutically acceptable carrier or excipient;

(5) a combination (C1) comprising an integrin binding pro-angiogenic agent and another angiogenic molecule;

(6) enhancing (M2) angiogenesis comprising administering C1 to a mammal where angiogenesis is desirable, to enhance angiogenesis in a mammal;

(7) enhancing (M3) angiogenesis comprising administering an integrin antagonist to a mammal where the angiogenesis is desirable, to enhance angiogenesis; and

(8) a combination (C2) comprising an integrin antagonist and another angiogenic molecule.

ACTIVITY - Vasotropic; vulnerary; angiogenic.

No supporting data.

MECHANISM OF ACTION - Angiogenesis-Stimulator.

To determine whether soluble L1 polypeptides can induce angiogenesis, 3 L1 GST fusion proteins that together span the entire extracellular domain of L1. The fusion proteins consists of Ig-like domains 1-3 and 4-6 and fibronectin like domains FN 1-5. The ability of these fusion proteins to induce angiogenesis was assessed in the chick chorioallantoic model. Results showed that the induction of a significant angiogenic response was produced by the fragment containing Ig-like domains 4 to 6. Such a response was not observed in equimolar amounts of the fibronectin-like domains of L1 (FN-1-5), and immunoglobulins 1-3 induced only a limited response. The response induced by Ig 4-6 was comparable to that induced by bFGF used at a concentration optimal for the induction of an angiogenic response.

USE - M1 is used to enhance angiogenesis in a mammal, such as a human (claimed), to treat disorders or diseases associated with deficient angiogenesis, such as ischemic diseases or wound healing disorders, by administering an integrin binding pro-angiogenic agent to the mammal.  
Dwg.0/4

L107 ANSWER 18 OF 18 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN  
ACCESSION NUMBER: 1993-182240 [22] WPIDS  
CROSS REFERENCE: 1990-009428 [02]; 1991-132637 [18]; 1991-238015 [32];  
1993-336910 [42]; 1997-401884 [37]; 2001-610491 [70];  
2003-438063 [41]; 2003-439103 [41]  
DOC. NO. CPI: C1993-080675  
TITLE: Prevention or reduction of dermal scarring - by  
administration of decorin or its functional equivalents

DERWENT CLASS: bi-glycan or fibromodulin.  
 B04 D16  
 INVENTOR(S): BORDER, W A; HARPER, J R; LONGAKER, M T; PIERSCHBACHER, M  
 D; RUOSLAHTI, E I; WHITBY, D J  
 PATENT ASSIGNEE(S): (LJOL-N) LA JOLLA CANCER RES FOUND; (REGC) UNIV  
 CALIFORNIA; (UTAH) UNIV UTAH; (WHIT-I) WHITBY D J  
 COUNTRY COUNT: 38  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9309800	A1	19930527	(199322)*	EN	73
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE					
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO RU SD US					
AU 9331385	A	19930615	(199340)		
NO 9401821	A	19940714	(199432)		
FI 9402244	A	19940706	(199435)		
JP 07504886	W	19950601	(199530)		
EP 667784	A1	19950823	(199538)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE					
AU 673506	B	19961114	(199702)		
EP 1230929	A1	20020814	(200261)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE					
EP 667784	B1	20030305	(200318)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE					
DE 69232946	E	20030410	(200332)		
ES 2188585	T3	20030701	(200347)		

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9309800	A1	WO 1992-US9871	19921113
AU 9331385	A	AU 1993-31385	19921113
NO 9401821	A	WO 1992-US9871	19921113
		NO 1994-1821	19940513
FI 9402244	A	WO 1992-US9871	19921113
		FI 1994-2244	19940513
JP 07504886	W	WO 1992-US9871	19921113
		JP 1993-509458	19921113
EP 667784	A1	EP 1992-925260	19921113
		WO 1992-US9871	19921113
AU 673506	B	AU 1993-31385	19921113
EP 1230929	A1 Div ex	EP 1992-925260	19921113
		EP 2002-10251	19921113
EP 667784	B1	EP 1992-925260	19921113
		WO 1992-US9871	19921113
	Related to	EP 2002-10251	19921113
DE 69232946	E	DE 1992-632946	19921113
		EP 1992-925260	19921113
		WO 1992-US9871	19921113
ES 2188585	T3	EP 1992-925260	19921113

# FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9331385	A Based on	WO 9309800
JP 07504886	W Based on	WO 9309800
EP 667784	A1 Based on	WO 9309800
AU 673506	B Previous Publ. Based on	AU 9331385
		WO 9309800
EP 1230929	A1 Div ex	EP 667784
EP 667784	B1 Related to Based on	EP 1230929
		WO 9309800
DE 69232946	E Based on	EP 667784



Based on WO 9309800  
ES 2188585 T3 Based on EP 667784

PRIORITY APPLN. INFO: US 1992-882345 19920513; US 1991-792192  
19911114

AN 1993-182240 [22] WPIDS

CR 1990-009428 [02]; 1991-132637 [18]; 1991-238015 [32]; 1993-336910 [42];  
1997-401884 [37]; 2001-610491 [70]; 2003-438063 [41]; 2003-439103 [41]

AB WO 9309800 A UPAB: 20030723

Prevention or redn. of scarring is claimed comprising administering decorin or a functional equivalent of decorin to a wound. The functional equivalent may be e.g. biglycan or fibromodulin.

Also claimed are: a **pharmaceutical compsn.** comprising decorin or its functional equivalents and a carrier, e.g. hyaluronic acid; the compsn. may further comprise an **RGD-contg.** polypeptide attached to a biodegradable polymer; a method of treating a pathology caused by a transforming growth factor (TGF)-beta regulated activity comprising contacting the TGF-beta with a purified polypeptide comprising a TGF-beta binding domain of a protein characterised by a leucine-rich **repeat** of about 24 amino acids, whereby the pathology-causing activity is prevented or reduced, the protein may be e.g. decorin, biglycan or fibromodulin.

USE/ADVANTAGE - Decorin binds and neutralises a variety of biological functions of TGF-beta, including the induction of extracellular matrix. Thus decorin can be used to prevent or reduce dermal scarring resulting from burns, skin injuries or surgery. The polypeptides can be used for treating TGF-beta pathologies such as rheumatoid arthritis, glomerulonephritic, arteriosclerosis, adult respiratory distress syndrome, cirrhosis of the liver, fibrotic cancer, fibrosis of the lungs, post-myocardial infarction, cardiac fibrosis, post-angioplasty restenosis, renal interstitial fibrosis or dermal fibrotic conditions (claimed)  
Dwg.0/19

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**WEST**[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 17 of 17 returned.****1. Document ID: US 20030162164 A1**

L8: Entry 1 of 17

File: PGPB

Aug 28, 2003

PGPUB-DOCUMENT-NUMBER: 20030162164  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030162164 A1

TITLE: Comparative phenotype analysis of cells, including testing of biologically active compounds

PUBLICATION-DATE: August 28, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bochner, Barry	Alameda	CA	US	
Morgan, Amy	Oakland	CA	US	

US-CL-CURRENT: 435/4; 435/287.1

<a href="#">Full</a>	<a href="#">Title</a>	<a href="#">Citation</a>	<a href="#">Front</a>	<a href="#">Review</a>	<a href="#">Classification</a>	<a href="#">Date</a>	<a href="#">Reference</a>	<a href="#">Sequences</a>	<a href="#">Attachments</a>
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<a href="#">Link</a>	<a href="#">Draw Data</a>	<a href="#">Image</a>
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**2. Document ID: US 20030119184 A1**

L8: Entry 2 of 17

File: PGPB

Jun 26, 2003

PGPUB-DOCUMENT-NUMBER: 20030119184  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030119184 A1

TITLE: Methods and compositions of bioartificial kidney suitable for use in vivo or ex vivo

PUBLICATION-DATE: June 26, 2003

## INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Humes, H. David	Ann Arbor	MI	US	

US-CL-CURRENT: 435/369; 604/5.01

<a href="#">Full</a>	<a href="#">Title</a>	<a href="#">Citation</a>	<a href="#">Front</a>	<a href="#">Review</a>	<a href="#">Classification</a>	<a href="#">Date</a>	<a href="#">Reference</a>	<a href="#">Sequences</a>	<a href="#">Attachments</a>
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<a href="#">Link</a>	<a href="#">Draw Data</a>	<a href="#">Image</a>
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**3. Document ID: US 20030087830 A1**

L8: Entry 3 of 17

File: PGPB

May 8, 2003

PGPUB-DOCUMENT-NUMBER: 20030087830

PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20030087830 A1

TITLE: Low molecular weight components of cartilage, complexes of metals with amino acids, DI-peptides and analogs thereof; processes for preparation and therapeutic uses thereof

PUBLICATION-DATE: May 8, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Dupont, Eric	Ste-Petronille, Ile d'Orleans		CA	
Lessard, Denis	Levis		CA	
Auger, Serge	St-Lambert		CA	
Dimitriadou, Violetta	Cap Rouge		CA	
Falardeau, Pierre	Sillery		CA	
Poyet, Patrick	St-Nicolas		CA	

US-CL-CURRENT: 514/19; 548/402, 556/116

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequence	Attachment
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Full	Draw Date	Image
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4. Document ID: US 20010041363 A1

L8: Entry 4 of 17

File: PGPB

Nov 15, 2001

PGPUB-DOCUMENT-NUMBER: 20010041363  
PGPUB-FILING-TYPE: new  
DOCUMENT-IDENTIFIER: US 20010041363 A1

TITLE: Methods and compositions of a BIOARTIFICIAL kidney suitable for use in vivo or ex vivo

PUBLICATION-DATE: November 15, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Humes, H. David	Arbor	MI	US	

US-CL-CURRENT: 435/325; 435/369

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequence	Attachment
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5. Document ID: US 6150164 A

L8: Entry 5 of 17

File: USPT

Nov 21, 2000

US-PAT-NO: 6150164  
DOCUMENT-IDENTIFIER: US 6150164 A  
**\*\* See image for Certificate of Correction \*\***

TITLE: Methods and compositions of a bioartificial kidney suitable for use in vivo or ex vivo

DATE-ISSUED: November 21, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Humes; H. David	Ann Arbor	MI		

US-CL-CURRENT: 435/400; 435/325, 435/347, 435/369, 435/371, 435/373, 435/395

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 6. Document ID: US 6083602 A

L8: Entry 6 of 17

File: USPT

Jul 4, 2000

US-PAT-NO: 6083602

DOCUMENT-IDENTIFIER: US 6083602 A

TITLE: Incontinent garments

DATE-ISSUED: July 4, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caldwell; J. Michael	Cardiff	CA		
Ellman; Peter	Olivenhain	CA		

US-CL-CURRENT: 428/77; 428/138, 428/78, 604/378, 604/381, 604/385.01

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 7. Document ID: US 6060270 A

L8: Entry 7 of 17

File: USPT

May 9, 2000

US-PAT-NO: 6060270

DOCUMENT-IDENTIFIER: US 6060270 A

TITLE: Methods and compositions for isolation and growth of kidney tubule stem cells, in vitro kidney tubulogenesis and ex vivo construction of renal tubules

DATE-ISSUED: May 9, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Humes; H. David	Ann Arbor	MI		

US-CL-CURRENT: 435/69.1; 424/93.1, 424/93.2, 424/93.21, 435/320.1, 435/325, 435/349, 435/350, 435/363, 435/364, 435/365.1, 435/366, 435/374, 435/383, 435/395, 435/455, 514/2, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 8. Document ID: US 6040251 A

L8: Entry 8 of 17

File: USPT

Mar 21, 2000

US-PAT-NO: 6040251

DOCUMENT-IDENTIFIER: US 6040251 A

TITLE: Garments of barrier webs

DATE-ISSUED: March 21, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caldwell; J. Michael	Cardiff	CA		

US-CL-CURRENT: 442/123; 128/849, 128/888, 2/114, 2/83, 2/901, 424/402, 424/404,  
428/305.5, 428/306.6, 428/308.4, 428/311.11, 428/311.51, 428/311.71, 428/315.5,  
428/907, 442/61, 523/103, 523/122, 602/48, 602/50, 604/367, 604/372

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 9. Document ID: US 6034220 A

L8: Entry 9 of 17

File: USPT

Mar 7, 2000

US-PAT-NO: 6034220

DOCUMENT-IDENTIFIER: US 6034220 A

TITLE: Chemical modification of repetitive polymers to enhance water solubility

DATE-ISSUED: March 7, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stedronsky; Erwin R.	San Diego	CA		

US-CL-CURRENT: 530/353; 530/350, 530/402, 530/408, 530/409, 530/410, 8/127.5,  
8/128.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 10. Document ID: US 5912116 A

L8: Entry 10 of 17

File: USPT

Jun 15, 1999

US-PAT-NO: 5912116

DOCUMENT-IDENTIFIER: US 5912116 A

TITLE: Methods of measuring analytes with barrier webs

DATE-ISSUED: June 15, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caldwell; J. Michael	Cardiff	CA		

US-CL-CURRENT: 435/5; 435/7.92, 436/518, 436/535

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 11. Document ID: US 5874164 A

L8: Entry 11 of 17

File: USPT

Feb 23, 1999

US-PAT-NO: 5874164

DOCUMENT-IDENTIFIER: US 5874164 A

TITLE: Barrier webs having bioactive surfaces

DATE-ISSUED: February 23, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caldwell; J. Michael	Cardiff	CA		

US-CL-CURRENT: 428/306.6; 424/278.1, 424/443, 424/499, 428/308.4, 428/317.1,  
428/422, 428/447, 442/76, 442/79, 442/82

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 12. Document ID: US 5856245 A

L8: Entry 12 of 17

File: USPT

Jan 5, 1999

US-PAT-NO: 5856245

DOCUMENT-IDENTIFIER: US 5856245 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Articles of barrier webs

DATE-ISSUED: January 5, 1999

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Caldwell; J. Michael	Cardiff	CA		
Ellman; Peter	Olivenhain	CA		

US-CL-CURRENT: 442/76; 128/849, 128/888, 424/404, 442/123, 442/152, 442/153,  
442/164, 442/79, 602/48, 602/50, 604/372, 604/374, 604/377

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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## 13. Document ID: US 5843781 A

L8: Entry 13 of 17

File: USPT

Dec 1, 1998

US-PAT-NO: 5843781

DOCUMENT-IDENTIFIER: US 5843781 A

TITLE: Implantable prosthetic vascular device having an adherent cell monolayer produced under shear stress

DATE-ISSUED: December 1, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ballermann; Barbara J.	Cockeysville	MD		
Ott; Mark J.	Baltimore	MD		

US-CL-CURRENT: 435/400; 424/424, 424/93.3, 424/93.7, 435/180, 435/363, 435/366,  
435/373, 435/395, 435/396, 435/402

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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14. Document ID: US 5808012 A

L8: Entry 14 of 17

File: USPT

Sep 15, 1998

US-PAT-NO: 5808012

DOCUMENT-IDENTIFIER: US 5808012 A

TITLE: Protein-enriched thermoplastics

DATE-ISSUED: September 15, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Donofrio; David M.	Scotts Valley	CA		
Stedronsky; Erwin R.	San Clemente	CA		

US-CL-CURRENT: 525/54.1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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15. Document ID: US 5760004 A

L8: Entry 15 of 17

File: USPT

Jun 2, 1998

US-PAT-NO: 5760004

DOCUMENT-IDENTIFIER: US 5760004 A

TITLE: Chemical modification of repetitive polymers to enhance water solubility

DATE-ISSUED: June 2, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Stedronsky; Erwin R.	San Diego	CA		

US-CL-CURRENT: 514/21; 530/353

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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16. Document ID: US 5696229 A

L8: Entry 16 of 17

File: USPT

Dec 9, 1997

US-PAT-NO: 5696229

DOCUMENT-IDENTIFIER: US 5696229 A

TITLE: Polypeptide with laminin cell adhesion and morphogenesis activity

DATE-ISSUED: December 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Laurie; Gordon W.	Charlottesville	VA		
Matter; Michelle L.	La Jolla	CA		
Chen; Lanlin	Charlottesville	VA		

US-CL-CURRENT: 530/326; 530/327, 530/328, 530/329, 530/330

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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17. Document ID: US 5686289 A

L8: Entry 17 of 17

File: USPT

Nov 11, 1997

US-PAT-NO: 5686289

DOCUMENT-IDENTIFIER: US 5686289 A

TITLE: Method and compositions of a bioartificial kidney suitable for use in vivo or ex vivo

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Humes; H. David	Ann Arbor	MI		
Cieslinski; Deborah A.	Ann Arbor	MI		

US-CL-CURRENT: 435/325; 435/369, 435/377, 435/397, 435/400, 514/2, 530/350, 530/399

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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